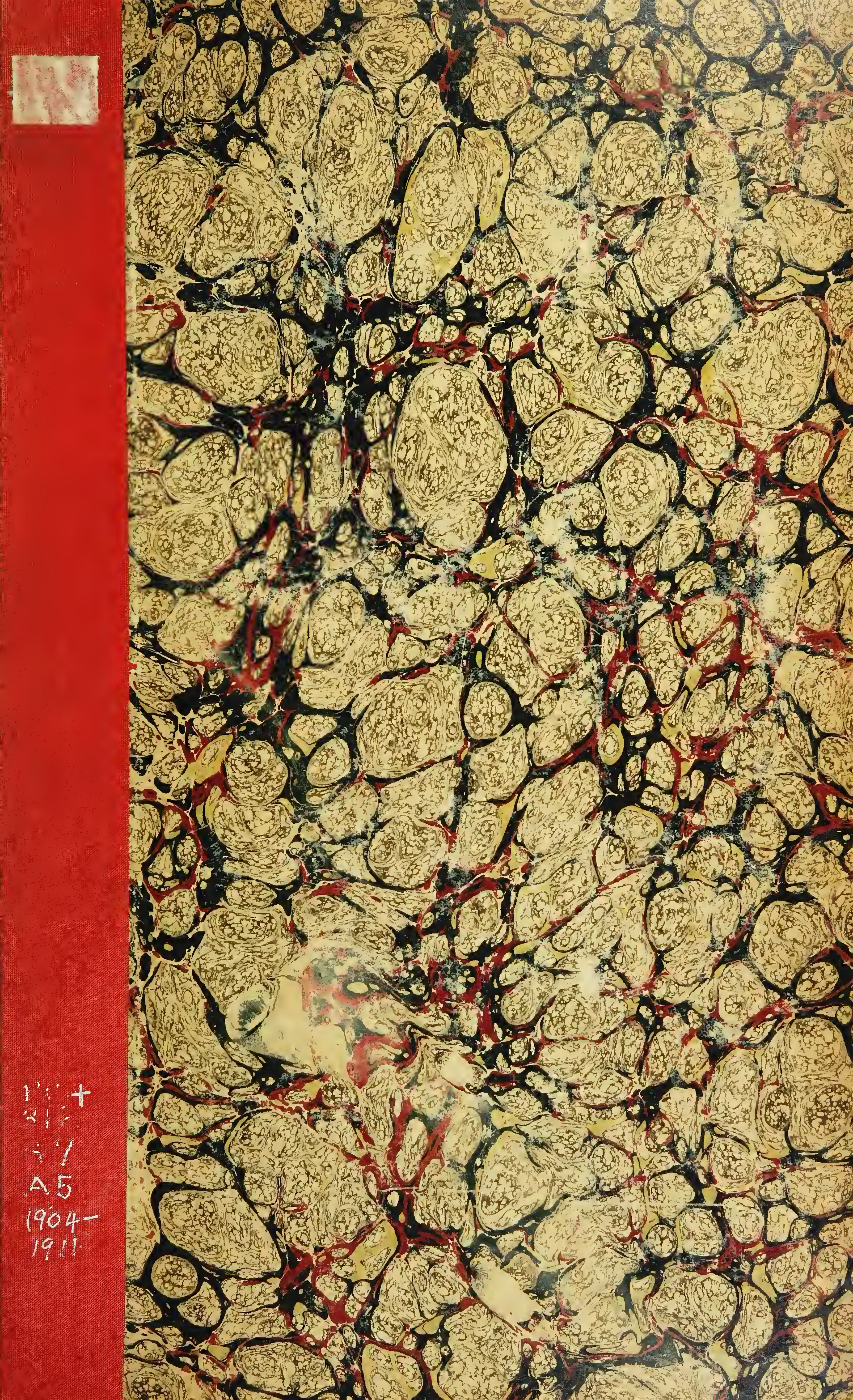

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ROYAL COMMISSION ON TUBERCULOSIS (HUMAN AND BOVINE).

INTERIM REPORT

OF THE

ROYAL COMMISSION

APPOINTED TO INQUIRE INTO THE RELATIONS OF

HUMAN AND ANIMAL TUBERCULOSIS.

Presented to both Houses of Parliament by Command of His Majesty.

LONDON:
PRINTED FOR HIS MAJESTY'S STATIONERY OFFICE,
BY WYMAN AND SONS, LIMITED, FETTER LANE, E.C.

And to be purchased, either directly or through any Bookseller, from
EYRE AND SPOTTISWOODE, East Harding Street, Fleet Street, E.C., and
32, Abingdon Street, Westminster, S.W.; or
OLIVER AND BOYD, Edinburgh; or
E. PONSONBY, 116, Grafton Street, Dublin.

1904.

[Cd. 2092.] *Price 1d.*

NEW ROYAL COMMISSION ON TUBERCULOSIS.

EDWARD R.

EDWARD THE SEVENTH, by the Grace of God of the United Kingdom of Great Britain and Ireland King, Defender of the Faith, To

Our Trusty and Well-beloved Sir MICHAEL FOSTER, Knight Commander of Our most Honourable Order of the Bath, Doctor of Medicine, Fellow of the Royal Society, Professor of Physiology in Our University of Cambridge ;

Our Trusty and Well-beloved GERMAN SIMS WOODHEAD, Esquire, Doctor of Medicine, Professor of Pathology in Our University of Cambridge ;

Our Trusty and Well-beloved SIDNEY HARRIS COX MARTIN, Esquire, Doctor of Medicine, Fellow of the Royal Society, Professor of Pathology at University College, London ;

Our Trusty and Well-beloved JOHN McFADYEAN, Esquire, Principal and Professor of Comparative Pathology and Bacteriology at the Royal Veterinary College ; And

Our Trusty and Well-beloved RUBERT WILLIAM BOYCE, Esquire, Professor of Pathology at University College, Liverpool.

GREETING :

Whereas We have deemed it expedient that a Commission should forthwith issue to inquire and report with respect to Tuberculosis :—

1. Whether the disease in animals and man is one and the same ;
2. Whether animals and man can be reciprocally infected with it ;
3. Under what conditions, if at all, the transmission of the disease from animals to man takes place, and what are the circumstances favourable or unfavourable to such transmission.

Now know ye, that We, reposing great trust and confidence in your knowledge and ability, have authorised and appointed, and do by these presents authorise and appoint you, the said Sir Michael Foster, German Sims Woodhead, Sidney Harris Cox Martin, John McFadyean, and Rubert William Boyce, to be Our Commissioners for the purposes of the said inquiry.

And for the better effecting the purposes of this Our Commission We do by these Presents give and grant unto you, or any three or more of you, full power to call before you such persons as you shall judge likely to afford you any information upon the subject of this Our Commission ; and also to call for have access to and examine all such books, documents, registers and records, as may afford you the fullest information on the subject, and to inquire of and concerning the premises by all other lawful ways and means whatsoever.

And We do by these Presents authorise and empower you, or any three or more of you, to visit and personally inspect such places as you may deem it expedient so to inspect for the more effectual carrying out of the purposes aforesaid.

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And We do further by these Presents will and ordain that this Our Commission shall continue in full force and virtue, and that you, Our said Commissioners, or any three or more of you, may from time to time proceed in the execution thereof, and of every matter and thing therein contained, although the same be not continued from time to time by adjournment.

And We do further ordain that you, or any three or more of you, have liberty to report your proceedings under this Our Commission from time to time if you shall judge it expedient so to do.

And Our further Will and Pleasure is that you do, with as little delay as possible, report to Us under your hands and seals, or under the hands and seals of any three or more of you, your opinion upon the matters herein submitted for your consideration.

Given at Our Court at Saint James's the Thirty-first day of August 1901; in the first Year of Our Reign.

By His Majesty's Command.

CHARLES RITCHIE.

To The King's Most Excellent Majesty.

May it please your Majesty,

We, your Majesty's Commissioners, appointed to inquire and report with respect to tuberculosis :—

1. Whether the disease in animals and man is one and the same;
2. Whether animals and man can be reciprocally infected with it;
3. Under what conditions, if at all, the transmission of the disease from animals to man takes place, and what are the circumstances favourable or unfavourable to such transmission;

humbly submit this Report on the progress which we have made in the inquiry.

The greater part of the above reference is directed to the view which had been expressed that the bacillus which gives rise to tuberculosis in the bovine animal is specifically distinct from the bacillus which gives rise to tuberculosis in the human being, and that therefore the presence of the bovine bacillus in the milk or flesh of the cow, consumed as food by man, is not to be regarded as a cause of tuberculosis in the latter. To this point we first turned our attention.

After duly considering the matter, we came to the conclusion that it would be desirable not to begin the inquiry by taking evidence, that is to say, by collecting the opinions of others (though this might be desirable at a later stage), but to attack the problem laid before us by conducting experimental investigations of our own.

The first line of inquiry upon which we entered may be stated as follows :—

What are the effects produced by introducing into the body of the bovine animal (calf, heifer, cow), either through the alimentary canal as food, or directly into the tissues by subcutaneous or other injection, tuberculous material of human origin, *i.e.*, material containing living tubercle bacilli obtained from various cases of tuberculous disease in human beings, and how far do these effects resemble or differ from the effects produced by introducing into the bovine animal, under conditions as similar as possible, tuberculous material of bovine origin, *i.e.*, material containing living tubercle bacilli obtained from cases of tuberculous disease in the cow, calf, or ox ?

We have up to the present made use, in the above inquiry, of more than twenty different 'strains' of tuberculous material of human origin, that is to say, of material taken from more than twenty cases of tuberculous disease in human beings, including sputum from phthisical patients and the diseased parts of the lungs in pulmonary tuberculosis, mesenteric glands in primary abdominal tuberculosis, tuberculous bronchial and cervical glands, and tuberculous joints. We have compared the effects produced by these with the effects produced by several different strains of tuberculous material of bovine origin.

In the case of seven of the above strains of human origin, the introduction of the human tuberculous material into cattle gave rise at once to acute tuberculosis, with the development of widespread disease in various organs of the body, such as the lungs, spleen, liver, lymphatic glands, etc. In some instances the disease was of remarkable severity.

In the case of the remaining strains, the bovine animal into which the tuberculous material was first introduced was affected to a less extent. The tuberculous disease was either limited to the spot where the material was introduced (this occurred, however, in two instances only, and these at the very beginning of our inquiry), or spread to a variable extent from the seat of inoculation along the lymphatic glands, with, at most, the appearance of a very small amount of tubercle in such organs as the lungs and spleen. Yet tuberculous material taken from the bovine animal thus affected, and introduced successively into other bovine animals, or into guinea-pigs from which bovine animals were subsequently inoculated, has, up to the present, in the case of five of these remaining strains, ultimately given rise in the bovine animal to general tuberculosis of an intense character; and we are still carrying out observations in this direction.

We have very carefully compared the disease thus set up in the bovine animal by material of human origin with that set up in the bovine animal by material of bovine origin, and so far we have found the one, both in its broad general features and in its finer histological details, to be identical with the other. We have so far failed to discover any character by which we could distinguish the one from the other; and our records contain accounts of the post-mortem examinations of bovine animals infected with tuberculous material of human origin, which might be used as typical descriptions of ordinary bovine tuberculosis.

The results which we have thus obtained are so striking, that we have felt it our duty to make them known, without further delay, in the present Interim Report.

We defer to a further Report all narration of the details of our experiments (and we may say that up to the present time we have made use of more than two hundred bovine animals), as well as all discussions, including those dealing with the influence of dose and of individual as well as racial susceptibility, with questions of the specific virulence of the different strains of bacilli, with the relative activity of cultures of bacilli and of emulsions of tuberculous organs and tissues, and with other points. In that Report we shall deal fully with all these matters, as well as with the question why our results differ from those of some other observers.

Meanwhile we have thought it our duty to make this short Interim Report, for the reason that the result at which we have arrived, namely, that tubercle of human origin can give rise in the bovine animal to tuberculosis identical with ordinary bovine tuberculosis, seems to us to show quite clearly that it would be most unwise to frame or modify legislative measures in accordance with the view that human and bovine tubercle bacilli are specifically different from each other, and that the disease caused by the one is a wholly different thing from the disease caused by the other.

In conclusion we desire to express in the strongest terms our appreciation of the most generous assistance given to the Commission by Sir James Blyth, who has placed unreservedly at our disposal his farm buildings and other accommodation at Stansted. By his action not only has the Nation been saved a very large necessary expenditure, but we have been able, by the help of the admirable arrangements made for us, to carry out our investigations in a manner which would have been impossible had the accommodation and equipment for our enquiry been provided entirely at the public cost.

And we wish also to thank our Secretary, Dr. E. J. Steegmann, and our observers, Drs. Louis Cobbett, A. Stanley Griffith, Eastwood, and Hutchens, as well as the rest of our Staff, for the able services which they have untiringly rendered to us.

(Signed) M. FOSTER, *Chairman.*
G. SIMS WOODHEAD.
SIDNEY MARTIN.
J. McFADYEAN.
RUBERT BOYCE.

EDWARD J. STEEGMANN, *Secretary.*

16th May 1904.

ROYAL COMMISSION ON TUBERCULOSIS (HUMAN AND BOVINE).

SECOND INTERIM REPORT

OF THE

ROYAL COMMISSION

APPOINTED TO INQUIRE INTO THE RELATIONS OF

HUMAN AND ANIMAL TUBERCULOSIS.

PART I.

REPORT.

Presented to both Houses of Parliament by Command of His Majesty.

LONDON:
PRINTED FOR HIS MAJESTY'S STATIONERY OFFICE,
By DARLING & SON, Ltd., 34-40, Bacon Street, E.

And to be purchased, either directly or through any Bookseller, from
WYMAN and SONS, Ltd., Fetter Lane, E.C., and
32, Abingdon Street, Westminster, S.W.; or
OLIVER & BOYD, Tweeddale Court, Edinburgh; or
E. PONSONBY, 116, Grafton Street, Dublin.

1907.

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NEW ROYAL COMMISSION ON TUBERCULOSIS.

EDWARD R.

EDWARD THE SEVENTH, by the Grace of God of the United Kingdom of Great Britain and Ireland King, Defender of the Faith, To

Our Trusty and Well-beloved Sir MICHAEL FOSTER, Knight Commander of Our most Honourable Order of the Bath, Doctor of Medicine, Fellow of the Royal Society, Professor of Physiology in Our University of Cambridge;

Our Trusty and Well-beloved GERMAN SIMS WOODHEAD, Esquire, Doctor of Medicine, Professor of Pathology in Our University of Cambridge;

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Our Trusty and Well-beloved JOHN McFADYEAN, Esquire, Principal and Professor of Comparative Pathology and Bacteriology at the Royal Veterinary College; And

Our Trusty and Well-beloved RUBERT WILLIAM BOYCE, Esquire, Professor of Pathology at University College, Liverpool.

GREETING:

Whereas We have deemed it expedient that a Commission should forthwith issue to inquire and report with respect to Tuberculosis:—

1. Whether the disease in animals and man is one and the same;
2. Whether animals and man can be reciprocally infected with it;
3. Under what conditions, if at all, the transmission of the disease from animals to man takes place, and what are the circumstances favourable or unfavourable to such transmission.

Now know ye, that We, reposing great trust and confidence in your knowledge and ability, have authorised and appointed, and do by these presents authorise and appoint you, the said Sir Michael Foster, German Sims Woodhead, Sidney Harris Cox Martin, John McFadyean, and Rubert William Boyce, to be Our Commissioners for the purposes of the said inquiry.

And for the better effecting the purposes of this Our Commission We do by these Presents give and grant unto you, or any three or more of you, full power to call before you such persons as you shall judge likely to afford you any information upon the subject of this Our Commission; and also to call for, have access to, and examine all such books, documents, registers, and records as may afford you the fullest information on the subject, and to inquire of and concerning the premises by all other lawful ways and means whatsoever.

And We do by these Presents authorise and empower you, or any three or more of you, to visit and personally inspect such places as you may deem it expedient so to inspect for the more effectual carrying out of the purposes aforesaid.

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And We do further by these Presents will and ordain that this Our Commission shall continue in full force and virtue, and that you, Our said Commissioners, or any three or more of you, may from time to time proceed in the execution thereof, and of every matter and thing therein contained, although the same be not continued from time to time by adjournment.

And We do further ordain that you, or any three or more of you, have liberty to report your proceedings under this Our Commission from time to time if you shall judge it expedient so to do.

And Our further Will and Pleasure is that you do, with as little delay as possible, report to Us under your hands and seals, or under the hands and seals of any three or more of you, your opinion upon the matters herein submitted for your consideration.

Given at Our Court at Saint James's the Thirty-first day of August, 1901; in the first Year of Our Reign.

By His Majesty's Command.

CHARLES RITCHIE.

TO THE KING'S MOST EXCELLENT MAJESTY.

May it please your Majesty,

We, your Majesty's Commissioners, appointed to inquire and report with respect to tuberculosis :—

1. Whether the disease in animals and man is one and the same;

2. Whether animals and man can be reciprocally infected with it;

3. Under what conditions, if at all, the transmission of the disease from animals to man takes place, and what are the circumstances favourable or unfavourable to such transmission;

humbly submit the following Further Report containing a detailed account of the results very briefly stated in the Interim Report which we had the Honour to submit to Your Majesty in May, 1904, and of the progress which has since been made in the inquiry.

From the brief historical sketch which we have given it will be seen that the term "tuberculosis" means the changes taking place in the animal body when it is invaded by the organism called the "tubercle bacillus." Hence the problem placed before us by the first term of our reference, namely, "whether the disease in animals and man is one and the same," may be stated in the following form.

The tubercle bacillus is an organism capable of living, not only within, but also outside the animal body; it may be cultivated on various artificial media. Like other organisms it exhibits certain morphological characters which may be observed by means of the microscope; it grows and multiplies in certain ways; and it possesses certain physiological properties, through which it acts upon, and is acted upon by, its environment, whether that environment be a living animal body or a lifeless artificial medium.

To determine therefore whether tuberculosis in man is one and the same as tuberculosis in animals other than man, we have to inquire not only whether the changes wrought in the human body by the tubercle bacillus are one and the same as those wrought in the bodies of animals other than man, but also whether in all respects, in its microscopical, cultural, and other physiological characters, the tubercle bacillus which causes tuberculosis in man is one and the same as the tubercle bacillus which causes tuberculosis in animals other than man. For it is known on the one hand that pathological changes apparently one and the same may be brought about by different micro-organisms, and on the other hand that micro-organisms behaving apparently in one and the same way outside a living body may, when introduced into a living body, bring about changes which are not one and the same. We have accordingly to study and compare the pathological changes characteristic of tuberculosis in man and of tuberculosis in animals other than man, and to study and compare the morphological, cultural, and other features of the tubercle bacillus which bring about these changes in the one and in the others.

Tuberculosis occurs in many if not all of our domesticated mammals, in the ox, pig, horse, sheep, cat, dog, and others. It has also been observed in many wild mammals, the monkey for instance, when kept in captivity. A disease, called avian tuberculosis, is known to occur in certain birds; and reptiles have been described as suffering from tuberculosis. Hence the phrase tuberculosis in "animals other than man" opens up a very wide field of inquiry. We have, however, in the first instance, thought it desirable to study the subject in its relation to tuberculosis occurring in bovine animals, since this part of the whole problem is of the more pressing practical importance. We shall consider tuberculosis in other animals afterwards.

In attempting to decide whether tuberculosis in the bovine animal is "one and the same" as tuberculosis in man we have, in accordance with what was said above, to inquire whether the bacillus of bovine tuberculosis is identical in its microscopical, cultural, and other characters with the bacillus of human tuberculosis, and whether the pathological changes brought about in a living body by the one are identical with those brought about by the other. The latter inquiry has led us to introduce the bacillus of human tuberculosis into the bovine body, and to compare the changes set up by that introduction with the changes set up in the bovine body by the bacillus of bovine tuberculosis. In making this comparison, we have found it necessary not to trust merely to such cases of bovine tuberculosis arising naturally as might come within our knowledge, but to introduce artificially the bacillus of bovine tuberculosis into healthy bovine animals. Indeed, in this way only could we make exact comparisons between the two cases.

We have therefore been led to carry on two parallel investigations, an investigation into the effects produced in the bovine body by the introduction of the bacillus of human tuberculosis, and an investigation into the effects produced in the bovine body by the introduction under similar conditions of the bacillus of bovine tuberculosis.

These two parallel investigations have been carried on at two separate establishments, Walpole Farm and Blythwood Farm, placed at our disposal by the generosity of Sir James Blyth. The two farms are more than a mile apart, and every care has been taken to keep the work carried on at the one farm so distinct from that carried on at the other as to preclude all possibility of the one being infected from the other. A detailed description of the two establishments and a general account of the procedure which we have adopted in our inquiries will be found in the Introduction.

We have had constantly in mind, and have done our best to avoid, errors which might be introduced on the one hand by the occurrence of spontaneous tuberculosis in the animals used for experiments, and, on the other hand, by contamination taking place in the course of an experiment; and we have rigidly excluded all experiments in which any suspicion arose of the one or of the other. By making use chiefly of Jersey cattle, which are remarkably free from tuberculosis, we have been able to reduce to a minimum errors arising from spontaneous tuberculosis in bovines; and, in addition, each animal was tested with tuberculin before being used. In the case of monkeys the risk of error from spontaneous tuberculosis was much greater, and we have had to exclude several experiments in which there was reason to suppose that the tuberculosis found was not artificially produced. In the Appendix will be found an account of the few cases of spontaneous tuberculosis which we met with in the rabbits, guinea-pigs, and other animals obtained for the purpose of experiments, and of the cases, occurring in various animals, which we have excluded by reason of the possibility of contamination having in some way or other taken place in the course of the experiments.

It will be convenient to give first an account of the conclusions to which we have been led by our studies of bovine tuberculosis.

BOVINE TUBERCULOSIS.

2. We have made use, up to the present time, of tuberculous lesions from thirty cases of tuberculosis occurring naturally in the ox; to these we refer individually by number, calling them B. I. to XXX.

The tubercle bacillus was introduced into the animal used for experiment in the form either of an *emulsion of tuberculous lesions*, or *of a culture grown on an artificial medium and suspended in innocuous fluid.* In five of the viruses we have made use both of emulsion and of culture from the same lesions, and have been able to compare the results of the two.

For the experiments on bovine animals we have in the great majority of cases, as stated above, used Jersey calves, varying in age from three weeks to four or five months; but we have also at times used adult animals of the same breed, and also animals of the shorthorn breed. The results which we are about to describe must be understood as obtained with Jersey calves unless the contrary is stated.

THE EFFECTS OF INTRODUCING THE BACILLUS OF BOVINE TUBERCULOSIS INTO THE BODY OF THE BOVINE ANIMAL.

3. We have adopted two chief methods of introduction: (1) *Feeding,* (2) *Injection into the tissues.* We considered the desirability of making use of a third method, viz., the introduction of the bacillus into the lungs by the air passages; but decided not to adopt this method, at least in the first instance.

Injection into the tissues we carried out in three ways: (*a*) *subcutaneous injection*—the injection with a syringe of the emulsion or culture into the connective tissue beneath the skin, the place chosen for injection being, in nearly all cases, the side of the neck, and generally the left side; (*b*) *intravenous injection*—the injection with a syringe of the emulsion or culture into the interior of a vein (nearly always the jugular vein) and so into the blood stream; (*c*) *intramammary injection*—the injection with a syringe of the emulsion or culture through the teat canals into the milk cisterns.

We were led by our experience to adopt the subcutaneous method as our main method. We employed the intravenous and the intramammary methods for special objects only.

We will describe first the results obtained by subcutaneous injection, with the accompanying results of intravenous and intramammary injection, treating separately afterwards the results of feeding.

The Effects of Subcutaneous Injections.

4. In some cases the effects of the injection of the bacillus are very severe. We may briefly describe as follows what may be called the full effects.

At or near the seat of injection (in the neck) a swelling of varying size and increasing with varying rapidity makes its appearance. This may remain firm and hard to the end, or, especially when cultures are used, may form in the interior a cavity containing serous fluid; this in some cases discharges externally. The changes thus brought about we speak of as the "local lesion;" this may attain very considerable dimensions. Very soon after the injection the nearest lymphatic gland to the seat of injection, namely, the prescapular, may be felt from the outside to be enlarged; the enlargement progresses with varying rapidity, and a tumour of very large dimensions may be formed. A similar enlargement of the prepectoral lymphatic gland may similarly be recognised by touch.

Very soon, about the twelfth day, the temperature rises and the animal becomes ill. It loses flesh, respiratory troubles often make their appearance, and within a period varying from about twenty to fifty days the animal dies or is so ill that it has to be killed.

A post-mortem examination discloses the following. The local lesion is a mass of caseous tubercle, infiltrating the adjoining skin and muscles, and sometimes forming an abscess. The prescapular gland is a mass of caseous tubercle as is also the prepectoral gland, and as are also to a less but variable extent the thoracic and mediastinal glands. Tubercles more or less caseous are found in very many, sometimes in all, the other lymphatic glands. The lungs, spleen, liver, and also the kidneys are studded with tubercles, many of them caseous. Tubercles are found in the pleura, on the omentum, on the peritoneal surface, and in the intestinal walls.

The result then of the subcutaneous injection (into the neck) of an adequate number of bacilli is an *acute generalised progressive tuberculosis,* ending fatally within a few weeks. The tuberculous lesions are first obvious in the local lesion; the infection appears to proceed by way of the lymphatics to the nearest lymphatic gland, the prescapular and prepectoral, and to advance thence to the thoracic and mediastinal glands. Our experiments show that, with large doses given subcutaneously, tubercle bacilli are found at an early period (within twenty-four hours) in the blood stream; they are thus carried to all parts of the body and set up a widely distributed disease.

5. In other cases the effects of the injection of the bacillus are different. The local lesion, never very large and always circumscribed, after a while diminishes. The prescapular gland, after enlarging somewhat, diminishes again.

The animal may have a rise of temperature, and some disturbance of health; but these pass away, the animal increases in weight, and seems quite well.

When the animal, thus apparently in good health, is killed, an examination of the body discloses the following. The local lesion is a circumscribed mass of tuberculous tissue; but this is largely calcareous and otherwise presents features shewing that the lesion is in a *retrogressive* condition. The prescapular gland may also show tuberculous lesions, but these also are retrogressive and usually calcareous. In some cases no further disease is found in the rest of the body, but in other cases small or even minute tubercles may be found in the lungs or other organs; these tubercles, however, are often largely calcareous, and in all cases have undergone marked retrogressive change. Obviously in such cases the injection of the tubercle bacilli does set up tuberculous processes at the seat of injection, the disease spreading thence to the nearest lymphatic glands, and small foci of tubercle are started in various parts of the body. But in the local lesion and elsewhere the tuberculous processes, instead of, as in the other cases, progressing rapidly, are soon arrested; the action of the bacilli is met and overcome by the action of the tissues; the disease retrogresses and tends to disappear.

Between these two extreme cases, that of the rapidly fatal widespread progressive tuberculosis and that of the scanty tuberculosis soon retrogressing and not permanently injuring the health of animal, various intermediate stages have been observed by us. The mischief set up may be widespread and may progress to such an extent as to affect seriously the health of the animal, but after a while it retrogresses and the animal apparently recovers its health. We need not, however, dwell now on these cases, the details of which will be found in the Appendix. What we chiefly desire to point out now is that the bovine bacillus may, when injected subcutaneously, give rise either to a general progressive or to a limited retrogressive tuberculosis. As we shall see, bacilli from the same source may give rise to the one result in one animal and to the other in another.

6. Whether the one result or the other is obtained depends, in the first instance, on the dose—that is to say, on the number of bacilli injected. This is seen clearly in the cases in which the bacillus was injected in the form of culture.

Of 20 different viruses which were tested on bovine animals, 18 in doses of 50 mgrs. of culture always* produced a fatal generalised progressive tuberculosis, whether the culture was obtained from the original material or had been passed through other animals, whether the culture was a primary one or had been subcultured through several generations, and though the age of the culture varied from 71 to 1,002 days. In the case of 5 out of the 20 viruses doses of 10 mgrs. were used; the result was in the case of each virus, though not of each animal, a generalised progressive tuberculosis. In a number of other experiments with one or other of the same viruses, in one instance 25 mgrs., in another 12·5 mgrs., in four instances 10 mgrs., and in one instance 5 mgrs., produced a similar generalised progressive tuberculosis.

But when, in two instances, a dose of 0·02 mgrs. and of 0·01 mgrs. was used the result was in each case a limited retrogressive tuberculosis.

The results obtained by the injection of emulsions were much more varied (*see* Dr. Martin's Memorandum). As a rule emulsions are much more effective than cultures. Thus, with one exception (Calf 160, Virus B. II.), the number of bacilli injected in the form of emulsions (so far as could be ascertained) was far below that contained in 0·01 milligramme of culture, which is probably about 50,000,000; yet, in some cases, these smaller doses gave rise to a generalised progressive tuberculosis equal in intensity to that produced by 50 milligrammes of culture. In other cases, however, similar doses gave rise merely to a limited retrogressive tuberculosis, and in yet other cases to tuberculosis of intermediate grades more or less general, and more or less retrogressive. Certain conditions seem to exist in cultures and in emulsions, which determine that the same number of bacilli are much more effective in the latter than in the former, and more effective in some of the latter than in others. In spite, however, of the influence of these conditions (the nature of which we need not attempt to discuss here) we are able to recognise that in emulsions, as in cultures, the larger dose produces the greater effect.

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* In one animal, Calf 240, Virus B. VI., the disease, though generalised, was not fatal within the 90 (days) period of observation.

One other condition besides dose determining the result deserves notice.

Two calves (130 and 124) each received, in the form of an emulsion, the same estimated dose (9,000 bacilli) of the same emulsion of Virus I. Yet Calf 124 died of general progressive tuberculosis, while Calf 130, killed in apparent good health, showed only a very limited retrogressive tuberculosis. Not only with emulsions from bovine sources, but also with those from human sources, and with cultures also when doses smaller than 50 mgrs. were given, we have found similar striking differences between the effects of the same dose of the same material on two animals of about the same age and weight, and apparently in the same condition of health.

The effect produced in a tissue of a living animal by the lodgment of a group of tubercle bacilli is the result of a combat between the pathogenic energies of the bacilli, and what has been called the "resistance" of the tissues. According as the one or the other is the stronger, a tuberculosis more or less progressive is set up, or a tuberculosis after being set up retrogresses with greater or less rapidity, or no tuberculosis at all is set up. We are led to the conclusion that in the case of the calves just mentioned, while the pathogenic energies of the bacilli injected were the same, in the two cases, the powers of resistance of Calf 130 were far greater than those of Calf 124; and so in other cases.

7. The results above mentioned were obtained on calves. We have also made observations (*see* Dr. Martin's Memorandum) on the effects of the bovine bacillus on adult animals. Making every allowance for the difficulties just stated attending the quantitative estimation of the pathogenic powers of a dose of bacilli, our results show that on the whole the same dose of bacilli produces less effect on an adult animal than on a young calf. This result we may explain as due to the powers of resistance of the tissues increasing with age. We have made a few observations on animals of a breed other than the Jersey on which all the observations referred to above were made. These are, however, at present too few to permit us to draw any conclusions as to the influence of breed on the powers of resistance.

8. Each of the twenty-one bovine viruses injected subcutaneously, when the dose was adequate, produced the full effect of generalised progressive tuberculosis; using here, and subsequently in this Report, the term "virulence" to denote quantitatively the power to produce tuberculous lesions, we may say that each of them possessed a high degree of "virulence." The question naturally arises, were they all equally virulent or was one more virulent than another, that is to say, did the same does of bacilli produce in the case of one virus pathogenic effects greater than those produced in the case of another virus? We cannot at present give a definite answer to this question. It is true that when 50 mgrs. of culture are used, we can find no striking differences between the several viruses. But 50 mgrs. is an enormous dose and must override differences which, even if they exist, cannot be expected to be very great. We have at present no series of completed observations which will enable us rightly to determine virulence quantitatively; but we are making observations directed to this point, and hope to be able to come to a conclusion later on.

The Effects of Intravenous and Intramammary Injections.

9. With intravenous injection, the bacilli thrown into the venous system are at once carried to the lungs, where a certain large proportion of them are arrested; the remainder are distributed over the body. This method of injection, though useful for certain special purposes, as will be seen when we come to discuss the effects of tubercle bacilli derived from a human source, did not appear to us so generally advantageous as the method of subcutaneous injection, and in studying the effects of bovine tubercle bacilli we have made very little use of it.

We have, however, several times injected both emulsions and cultures into the udder, introducing the material through the teat canals into two quarters of the udder and leaving two quarters for comparison. The most striking facts observed are as follows :—

A very large amount of tuberculous disease may be set up in the injected quarters of the udder and yet the disease may not spread to the other quarters or into the body beyond the supramammary lymphatic gland connected with the injected quarters. In such cases the disease may after a while retrogress or may lead to the death of the animal, apparently owing to poisonous (toxic) substances being absorbed from the affected udder.

In other cases the disease may spread to the uninjected quarters, and over the body generally, causing death by general progressive tuberculosis.

The cows thus affected with tuberculosis of the udder have been utilised in obtaining tuberculous milk for experiments.

The Effects of Feeding Calves with the Bacillus of Bovine Tuberculosis.

10. In each of six cows whose udders had been made tuberculous by intramammary injection the calves were allowed to suck for varying periods, beginning the day after, or a few days after the injection. The number of bacilli ingested could not, of course, be determined. In one case only was general tuberculosis produced. In all the other five calves killed after being kept alive from 74 to 363 days the tuberculosis was for the most part limited to the intestines and mesenteric glands, a few nodules in some cases being found in the ileo-cœcal, portal, or other glands, and in the liver or other internal organs; the lesions had the retrogressive character of being calcareous.

Fourteen calves, varying in age from three-and-a-half weeks to two months, were fed with tuberculous milk, six from one source eight from another, the number of bacilli thus ingested varying from one to ten millions and the experiments taking from thirty-six to a hundred and twenty-seven days. None of these calves showed when killed anything more than tuberculosis limited to the intestine and to the mesenteric or ileo-colic glands; in one case tuberculous lesions were found in the pharyngeal glands only.

These cases show that feeding with the bacillus of bovine tuberculosis does not so readily set up general progressive tuberculosis in the calf as does inoculation.

Assuming that some only, and possibly few only, of the bacilli entering the mouth were absorbed by the intestine (or from the pharynx), we may attribute the smallness of the effect to the smallness of the dose actually effective. The results of feeding might then be considered as parallel to the effects of the subcutaneous injection of very small doses. Yet the calves which sucked their tuberculous mothers for many days probably ingested no inconsiderable number of bacilli (though the exact number is unknown) without producing, save in one case only, anything more than a limited and retrogressive tuberculosis.

THE EFFECTS PRODUCED BY THE BACILLUS OF BOVINE TUBERCULOSIS IN ANIMALS OTHER THAN BOVINES.

Guinea-Pigs.

11. *Inoculation.*—In these animals an exceedingly small dose of bovine tubercle bacilli injected subcutaneously or intraperitoneally readily produced generalised progressive tuberculosis. Indeed, as is well known, this animal can be safely used in this way as a test for the presence of the tubercle bacillus when this cannot be found by microscopic search.

Feeding.—Generalised progressive tuberculosis was also readily produced by feeding, though the result was not so certain as when the method of inoculation was used.

Rabbits.

12. *Inoculation.*—The bacillus of bovine tuberculosis, in the form either of culture or emulsion, when injected subcutaneously, intraperitoneally, or intravenously, always produced a generalised progressive tuberculosis, and that even when given in a very small dose.

Feeding.—Generalised progressive tuberculosis was also set up in the rabbit by feeding, though not so readily as in the case of the guinea-pig.

Pigs.

13. *Inoculation.*—Our observations show that generalised progressive tuberculosis may readily be set up in the pig by the subcutaneous injection of even an exceedingly small dose of bovine tubercle bacilli. It was, in one case, produced by the injection of an emulsion containing so few bacilli that these could not be detected by microscopic search.

Feeding.—Pigs were also very readily made tuberculous by feeding. Thus, even so small a dose as 0·1 milligramme of culture produced generalised progressive tuberculosis (Pig 108), and a quantity of milk from a tuberculous udder containing not more than 10,000 bacilli produced in each of two animals tuberculous disease in the mesenteric and ileo-colic glands (Pigs 58, 60).

These animals, especially when young, are extremely susceptible to the bacillus of bovine tuberculosis.

Goats.

14. *Inoculation.*—Subcutaneous injection of the bacillus of bovine tuberculosis, either as emulsion or as culture, produced generalised progressive tuberculosis, fatal when the dose was large, but not fatal with smaller doses.

Feeding.—Though a generalised progressive tuberculosis was sometimes produced by feeding, the result was at other times a tuberculosis limited for the most part to the mesenteric and adjoining glands.

Dogs.

15. *Inoculation.*—The few observations which we have made show that in these animals generalised progressive tuberculosis may be set up by the intraperitoneal injection of the bacillus of bovine tuberculosis; subcutaneous injection had a very limited effect.

Feeding.—Feeding with the bacillus generally produced not more than a tuberculosis limited to the mesenteric or adjoining glands, though with very young animals the result was occasionally a generalised tuberculosis.

Cats.

16. *Inoculation.*—Our experiments on these animals show that generalised progressive tuberculosis may be set up in them by the subcutaneous or intraperitoneal injection of the bacillus of bovine tuberculosis, and that this occurs more readily than with dogs. When kittens were employed the generalised progressive tuberculosis set up was characterised by the presence of an enormous number of bacilli widely disseminated over the body.

Feeding.—With adult cats the results were very similar to those obtained with dogs.

Rats.

17. *Inoculation*—The effects of the subcutaneous or intraperitoneal injection of the bacillus of bovine tuberculosis, either as emulsion or culture, into these animals are peculiar. With small or moderate doses, and in some cases even with large doses, the animals may seem not to be affected, and when killed show no tuberculous lesions at all, or at most very few, and these extremely limited. In some cases, in which the dose was a very large one, the animal did die, but did not exhibit the lesions of generalised progressive tuberculosis. Tubercle bacilli were abundant in the tissues (and were found also in the blood), but were unable to give rise to the tissue changes which constitute tuberculous lesions. In the non-fatal cases also bacilli were found in abundance in the tissues. It would seem that in this animal the tubercle bacillus, when introduced, can readily multiply, but cannot give rise to tuberculous tissue changes. When present, however, in sufficient quantity, the bacillus can bring about physiological changes resulting in the death of the animal.

We have not made any large number of observations on mice; but these animals appear to resemble rats in their reactions to the bovine bacillus.

Feeding.—In none of twenty-six rats, fed largely for some time on tuberculous milk or tuberculous organs, were definite tuberculous lesions found.

Monkeys.

18. The animals used were either Rhesus monkeys (*Macacus Rhesus*) or Baboons (*Papio porcarius*), or Lemurs. As stated in § 1, we have taken every care that every monkey operated on should if possible be free from tuberculosis, and we have further rigorously excluded the cases in which there could be any doubt as to whether the tuberculosis found after death was really due to the bacilli administered.

Inoculation.—We have produced generalised progressive tuberculosis by the subcutaneous (and also by intravenous) injection of the bacillus of bovine tuberculosis in the form of emulsion and of culture. In one of these cases (Monkey 142), a fatal generalised progressive tuberculosis was produced by so small a dose as 0·001 mgr. of culture subcutaneously injected.

Feeding.—Not only was generalised progressive tuberculosis produced in Rhesus monkeys by feeding them with large, though undetermined, doses of bacilli given as tuberculous milk, but the same result was obtained by feeding with a single small dose, namely, 1 mgr. of culture.

We have also produced generalised progressive tuberculosis in Baboons by feeding with tubercle bacilli. This result was readily obtained with 1 mgr. of culture, and in two cases occurred with the small dose of one million bacilli given as tuberculous milk.

In the case of two Lemurs progressive tuberculosis resulted from feeding with 1 mgr. of culture.

Anthropoid Apes.

19. *Inoculation.*—A chimpanzee received by subcutaneous injection 1 mgr. of culture of Virus B. IV., and died in fifty-five days of generalised progressive tuberculosis. The result was so clear and decided that it did not seem necessary to repeat any injection experiments.

Feeding.—A chimpanzee (6) was fed for a week with tuberculous milk, the number of bacilli given being estimated roughly to be about 100 millions. It was killed when very ill, 100 days later, and showed generalised progressive tuberculosis; the intestines and associated glands were tuberculous, and there were also tubercles in the lungs, thoracic glands, spleen, and kidneys.

Another chimpanzee (8) received 10 million bacilli, tuberculous milk being the medium. It died 144 days afterwards, with tuberculous ulceration of the intestines, and caseous or caseo-calcareous lesions in the mesenteric and mesocolic glands. The tuberculosis was, therefore, limited.

A third chimpanzee (2) received 1 mgr. of a culture of Virus B. IV. It died in fifty-six days of generalised progressive tuberculosis with miliary tubercles in the lungs.

A fourth chimpanzee (14) received 1·1 mgr. of a culture of Virus B. IX. It died in 63 days of generalised progressive tuberculosis, the intestines and mesenteric glands being very severely affected.

It is clear that the bacillus of bovine tuberculosis will, either by feeding or by inoculation, produce, in even a small dose, generalised progressive tuberculosis in the anthropoid ape, an animal so nearly related to man.

Summary of the Effects of the Bacillus of Bovine Tuberculosis.

20. The results thus obtained by the study of the effects of the bacillus of bovine tuberculosis may be summarised as follows.

The bacillus of bovine tuberculosis introduced subcutaneously into the body of a bovine animal as an "emulsion" or as a "culture" may produce (1) a fatal generalised progressive tuberculosis; or (2) a limited retrogressive tuberculosis; or (3) effects intermediate between the above two.

One factor determining the amount of disease produced is the dose, that is to say, the number of bacilli injected, the larger number producing the greater effect. But in some instances the same quantity of the same emulsion or culture, presumably containing about the same number of bacilli, injected in the same way into two animals of about the same size and age, produced in one animal a much greater effect than in the other. This we attribute to the former animal being more "susceptible" to the bacillus, the tissues having less power of "resistance" than in the latter animal. Hence it is not the absolute dose, the absolute number of bacilli, which supplies a determining factor, but the dose in relation to the susceptibility of the animal.

Again, the effects of emulsions are consistently greater than are those of cultures estimated to contain the same number of bacilli. Certain conditions obtain either in the bacilli themselves or in the medium in the midst of which the bacilli are living whether in a culture or in an emulsion; and these bring it about that the same number of bacilli are more effective in the one case than in the other.

It will be understood, therefore, that we are not in a position to state absolutely what is the minimum dose which will produce a rapidly fatal generalised progressive tuberculosis in the bovine animal when injected subcutaneously. We have no means of quantitatively appreciating the other determining factors. Our results show that with each of the strains examined, 50 mgrs. of culture, roughly calculated to contain between 200,000 and 250,000 million bacilli, always produce the above fatal results. Such a dose overrides everything. A dose of 10 mgrs. culture, *i.e.*, 40,000 to 50,000 million bacilli, is often fatal but not always; this dose seems to leave room for the play of individual susceptibility. And the smallest dose of culture, 5 mgrs., which led to fatal progressive tuberculosis was calculated to contain 20,000 to 25,000 million bacilli, while the smallest determined effective dose of emulsion contained only 5,500 bacilli.

In striking contrast to the ease with which, an adequate dose being used, a rapidly fatal progressive tuberculosis is set up in the bovine body by tubercle bacilli subcutaneously injected, is the difficulty of producing the same result by feeding.

Turning now to the effect on animals other than bovine, our results show that the bacillus of bovine tuberculosis introduced either by injection or by feeding can set up general progressive tuberculosis in guinea-pigs, rabbits, pigs, goats, cats, dogs, and monkeys; and the list might probably be much extended. It can undoubtedly produce its full effects on animals other than bovine, though more readily on some kinds than on others.

The question naturally presents itself :—Is the bacillus of bovine tuberculosis as effective on these other animals as it is on the bovine animal? Now it is difficult to compare exactly the effects produced in one kind with those produced in another kind of animal. Where the two kinds differ widely in size we may affect an exactitude by using for comparison a unit of body weight, comparing, for instance, the effects of so many bacilli per kilo. of body weight; but such an exactitude is probably illusory. And in any case the conclusions arrived at on the point in question can only be approximate. The results which we have obtained do, however, point very strongly to the conclusion that the bacillus of bovine tuberculosis is not only as effective but even more effective in causing tuberculosis in some of the above animals than in the bovine animal itself. The fact that very few bacilli, though we do not know the exact limit of paucity, introduced subcutaneously into the body of a guinea-pig will so certainly produce generalised tuberculosis that the experiment may be trusted to test the presence of the bacillus, while many thousands at least are needed to ensure the same result in the bovine animal, cannot be explained by the mere difference in size between the two kinds of animals. We are driven to the conclusion that the guinea-pig is more susceptible to bovine tuberculosis than is the bovine animal itself. And this conclusion is supported by the fact that the bacillus of bovine tuberculosis given to the guinea-pig by the mouth, usually or at least often produced generalised tuberculosis even though the dose was small, whereas in the bovine animal feeding with even relatively large quantities produced as a rule only a limited local tuberculosis. Again, the difference in size between a pig and a calf is quite insufficient to explain the facts that general tuberculosis is much more readily produced by feeding and that, in subcutaneous injection, a much smaller dose gives rise to generalised tuberculosis in the former than in the latter. A similar conclusion may be drawn from the results obtained with monkeys. All these three kinds of animals—guinea-pigs, pigs, and monkeys—seem to be more susceptible to the action of the bacillus of bovine tuberculosis than is the bovine animal itself.

The bacillus of bovine tuberculosis is not so constituted as to act on bovine tissues only, for it can give rise to tuberculosis in many animals other than bovine;

it is not even so constituted as to act on bovine tissues with a special energy, for it can give rise to tuberculosis in some other animals as readily as, or even more readily than, in bovine animals themselves. We call it the bacillus of bovine tuberculosis merely because we find it most frequently in the bovine body, it being the cause of bovine tuberculosis.

The fact that the bacillus of bovine tuberculosis can readily by feeding as well as by subcutaneous injection give rise to generalised tuberculosis in the anthropoid ape, so nearly related to man, and indeed seems, so far as our few experiments go, to produce this result more readily than in the bovine body itself, has an importance so obvious that it need not be dwelt upon.

HUMAN TUBERCULOSIS.

21. We have studied the nature of the tuberculous material obtained from a large number (now amounting to sixty) of cases of the disease in man.

Our results have led us to divide these cases into two groups very clearly distinguished from each other by the properties and characters of the bacillus found in each.

Nearly all the cases fall readily into the one or the other group, and all the members of each group agree with each other in the features which we are about to describe. But some few cases present exceptional features by which they, in one respect or another differ from all the other cases, and it will be advantageous to consider these as forming a group by themselves.

Group I.

One group, which we will call Group I., is far smaller than the other, containing only fourteen cases out of the whole number. It will be convenient to consider this group first.

The viruses in this group were obtained in one case from sputum feeding, in three cases from tuberculous cervical glands removed by operation, and in ten cases from the lesions of cases of primary abdominal tuberculosis. All the cases of abdominal tuberculosis occurred in children and showed some distinctive feature demonstrating the primary origin of the disease. In some there was ulceration of the intestine, in others tuberculous peritonitis. All showed caseation of the mesenteric glands. In some cases the patient had died of generalised tuberculosis. In all cases the mesenteric glands were used for investigation, but in some of those in which there was generalisation of the disease, lesions remote from the mesenteric glands were also used, such as those occurring in the bronchial glands, lungs, and the meninges. (*See* Dr. Martin's Memorandum.)

The Effects produced on Bovine Animals.

The Effects of the Subcutaneous Injection of Emulsions.

22. We will consider first the effects produced by the subcutaneous injection into bovine animals of the tuberculous material of the several cases of this group in the form of emulsions either prepared directly from the original material or (H. 28 and H. 29) from the tuberculous organs of guinea-pigs infected with that material. Such emulsions were used in ten cases out of the fourteen, *i.e.*, in all but H. 38 and H. 49. In all cases the emulsion was injected into each of two animals, and these were young calves, except in the case of H. 7, one of the earlier cases studied, in which one of the animals was a heifer.

In all these ten cases the injection gave rise in one or both the animals used to a generalised tuberculosis. The disease so produced was in four cases (H. 14, 28, 29, 32) a fatal generalised progressive tuberculosis, the animal dying within fifty days or having to be killed in a dying condition; and this result was obtained in both the animals employed in each case. In one case (H. 19) only one of the two animals employed was affected to this fatal extent. In the other four cases the tuberculosis produced in one or both the animals employed, though generalised and progressive, was not severe enough to be fatal within the period of observation. And in three cases (H. 7, 19, 20) the effect produced in one of the two animals used was not more than a limited retrogressive tuberculosis.

The dose used, *i.e.*, the number of bacilli injected, was in some of the earlier cases not estimated, and varied largely in the others. Hence, putting wholly on one side for the present the question whether the bacilli in the several cases differed among themselves essentially in degree of virulence, that is, in the power to set up tuberculosis, the question naturally presents itself, Were the cases of lesser effect due to the dose given being too small in relation to the individual susceptibility of the animal employed?

That this was the explanation is strongly suggested by the fact that in the cases in which the original emulsion produced less than a fatal generalised progressive tuberculosis this greater effect was seen when the virus was carried on by the subcutaneous injection of emulsions from the animals originally infected to other animals (*see* for instance Calves 141, 105, in H. 7; Calf 191 in H. 10; Calf 271 in H. 19; Calves 335, 403, in H. 20).

The Effect of the Subcutaneous Injection of Cultures.

23. Definite proof of the above was afforded by the following experience.

We have seen that with bovine tuberculosis a large dose, 50 mgrs. of culture injected subcutaneously, produces fatal generalised progressive tuberculosis. Such a dose is, as we have said, large enough to overcome all resistance.

Cultures were prepared from the tuberculous material of each of the above ten cases, and also from that of each of the other two cases (H. 38 and 49) in which no emulsions had been used. The material employed for preparing the cultures was either the original material or the tuberculous organs of a guinea-pig or other animal infected with the original material.*

In each of the above fourteen cases the subcutaneous injection of 50 mgrs. of culture gave rise to a generalised progressive tuberculosis, the animal dying or being killed when very ill within fifty days; in nine out of the fourteen cases this result was obtained on both the two animals employed in each case; in one of the cases, the result in one of the animals employed was less severe.

We have seen that with the bacillus of bovine tuberculosis a smaller dose, 10 mgrs., injected subcutaneously while it sometimes produced fatal generalised progressive tuberculosis, sometimes gave rise to a less severe result; it would appear that in some calves the powers of resistance, while not great enough to withstand 50 mgrs., are able to withstand 10 mgrs. of the culture. We have tried the effect of a dose of 10 mgrs. of culture in all the cases of Group I., and the result has been wholly like that obtained with the bacillus of bovine tuberculosis; fatal generalised progressive tuberculosis was sometimes produced and sometimes not.

There can be no doubt, therefore, that the bacillus supplied to us from each of the cases of Group I. resembles the bacillus of bovine tuberculosis in being capable of producing a generalised progressive tuberculosis in the bovine body when injected subcutaneously.

Other Modes of Injection.

24. In some few cases of Group I. (H. 7, H. 10, H. 14, H. 28), the tuberculous material, either the original material or that material "passed" through the body of a guinea-pig, has been injected into the udder of a cow. The result has always been tuberculosis of the udder.

In the few cases in which the tuberculous material of Group I. has been injected intravenously into a bovine animal generalised tuberculosis has been the result.

We shall discuss separately the results which we have obtained by feeding bovine animals on tuberculous material of human source.

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* In the course of our inquiry, when dealing with tuberculous material, we have frequently had occasion to infect a guinea-pig, the susceptibility of the animal to the bacillus of tuberculosis being very great, and to use its tuberculous organs instead of, or in addition to, the original material. By this means we have been able to increase the number of bacilli and otherwise to obtain material better suited for the preparation of cultures. Sometimes we have found it advantageous thus to 'pass the virus' through more than one, through a succession of guinea-pigs.

EFFECT ON ANIMALS OTHER THAN BOVINES.

Rabbits.

25. In each of the cases of Group I. the bacillus in the form of culture, and also occasionally in the form of emulsion, has been injected sometimes subcutaneously, but most frequently intraperitoneally, into rabbits. The result has invariably been generalised progressive tuberculosis, usually fatal within a short period. And this result has been obtained not only with larger doses but also with doses so small as 0·01 mgr. We have not yet determined the minimal dose.

Rabbits fed on cultures of Group I. also developed generalised progressive tuberculosis.

Other Animals.

26. The bacillus of Group I. injected into the bodies of guinea-pigs has invariably, even in extremely small doses, given rise to generalised progressive tuberculosis; and guinea-pigs fed on cultures of Group I. also developed generalised progressive tuberculosis.

We have not made any large number of observations on other animals, but those which we have made show that the bacillus of Group I. will, in adequate dose, produce generalised progressive tuberculosis readily in pigs and goats, and even more readily in monkeys.

A dog inoculated intraperitoneally with 10 mgrs., and a chimpanzee inoculated subcutaneously with 1 mgr. of a culture of Group I. both died of generalised progressive tuberculosis.

27. We do not think it necessary to dwell in any further detail at present on the features of the effects thus produced by the bacillus of Group I. on bovine and other animals. We may say definitely and at once that these effects appear to us to be absolutely identical with the effects of the bacillus of bovine tuberculosis; we have wholly failed to discover any essential differences between the one and the other; both are equally virulent, *i.e.*, equally able to set up tuberculosis in bovine and other animals.

GROUP II.

28. This group, much larger than Group I., is made up of forty cases of very different kinds. In some cases the material consisted of cervical glands removed by operation. In eight others it consisted of mesenteric glands removed after death from cases in which the disease seemed to be of alimentary origin, and was either a general tuberculosis or a more localized affection. In others, again, ten in all, the material consisted of lungs or bronchial glands from cases in which the disease was of respiratory origin, mainly cases of pulmonary tuberculosis, mostly advanced, though generally in an acute phase. One case was that of a tuberculous kidney, another was that of a tuberculous testis. All the rest, nine in number, were cases of affections of the joints or bones. Our studies of these cases have led us to the conclusion that the bacillus in all of them possessed certain common features.

THE EFFECTS PRODUCED ON BOVINE ANIMALS.

The Effects of the Subcutaneous Injection of Emulsions.

29. When the bacillus is injected in the form of an emulsion, the effects, as might be expected from what we have seen in connection with the bacillus of bovine tuberculosis or of Group I., vary to a considerable extent.

A very common effect is as follows :—

1. A local lesion, consisting of a larger or smaller mass of tuberculous tissue in a condition more or less markedly retrogressive, and presenting on section, even to the naked eye, a very distinctive appearance widely differing from that of the local lesion seen in bovine tuberculosis or in Group I. It does not infiltrate the surrounding tissues, but is distinctly circumscribed by a zone of fibrous tissue, is frequently softened in the interior, and contains serous fluid.

2. More or less tuberculous deposits, in a distinctly retrogressive, frequently calcareous condition, in the nearest lymphatic glands, prescapular and prepectoral.

In some cases the affection of the prescapular or prepectoral glands was extensive, though always more or less retrogressive; in other cases it was slight; and in some cases it was wholly absent, the only effect of the injection being a local lesion of varying magnitude. In some few cases even the local lesion disappeared, so that the injection of the tuberculous material left no permanent visible effects whatever.

We may interpret these results in the following way.

When the emulsion of tuberculous material is lodged in the subcutaneous tissue of the neck the bacilli set up the process of tuberculosis. This proceeds to a greater or less extent, determined by the relation of the virulence, that is to say, the pathogenic powers of the bacilli to the powers of resistance of the tissues. In all cases the latter, after a varying period, gain the victory; a wall of non-tuberculous tissue surrounding and limiting the central tuberculous mass is formed, the process of tuberculosis in the central mass itself is arrested, the spread of the bacilli from that mass ceases, and the tubercle already formed undergoes calcareous degeneration, or a process of softening.

Meanwhile some of the bacilli from the local lesion have invaded the nearest lymphatic gland (prescapular, &c.), probably by way of the lymphatics, and set up tuberculosis there. But here also after a while the powers of resistance of the tissues gain the upper hand, and the tubercle, ceasing to increase, becomes retrogressive and degenerates.

Besides the mischief thus set up in the local lesion and the adjoining lymphatic glands, we observed in nearly half the cases a few scattered tubercles in a retrogressive condition in various organs, such as the lungs, liver, and distant lymphatic glands. In two exceptional cases these scattered tubercles were numerous and conspicuous, but as a rule they were minute, so minute indeed that their presence might easily be overlooked. In many cases no such tubercles could be found at all.

We have ascertained experimentally that, as in the case of the bacilli of bovine tuberculosis, when bacilli of this group are injected subcutaneously, in the neck, for instance, in an adequate dose, a certain number enter the blood stream within two days, and are then distributed all over the body. Groups of them are, in consequence, lodged here and there in various organs. These groups, if the pathogenic powers, that is, the "virulence" of the bacillus, be great enough, start a formation of tubercule; but, in all the cases in which we are speaking, the resistance of the tissues is great enough to overcome eventually the pathogenic action of the bacillus, the process of tuberculosis is arrested, and the small lesion which has already been formed becomes fibrous and calcareous or disappears.

The Effects of the Subcutaneous Injections of Cultures.

30. In the foregoing experiments with emulsions the dose was, in some cases, undetermined, and in other cases small. Hence the absence of a severe effect might be attributed to the dose being too small. We have therefore in all the above cases studied the effects of the subcutaneous injection of a measured dose of culture; and we have purposely chosen a very large dose, namely, 50 mgrs. or, in some cases, a still larger dose, so as to bring out clearly the maximum effect of the bacillus. The cultures used, grown on serum, were twenty-one days old. The results have been far more constant than have been those obtained with the emulsions. In spite of the very large dose in no case has the injection of a culture given rise to more than a limited retrogressive tuberculosis: to a circumscribed retrogressive local lesion, very frequently softened in the interior, to a retrogressive tuberculosis of the nearest lymphatic glands, and to a few small scattered retrogressive tubercles in various organs. And in some cases no such scattered tubercles could be found.

We have also given much larger doses (in two cases as much as 3,000 mgrs.) of cultures grown on serum, glycerin-serum broth, or glycerin-broth without producing results more severe than the above.

31. In all the cases of Group II., therefore, the bacillus, even given as a culture in very large doses, did not produce generalised progressive tuberculosis, when injected subcutaneously into bovine animals. This result was obtained not only with tuberculous material supplied from cases of phthisis and other pulmonary diseases, with tuberculous material supplied from cases of joint and bone affection, but also with tuberculous material supplied as mesenteric and cervical glands, that is to say, from cases in which, presumably, the infection took place by way of the alimentary canal, cases so far similar to those which furnished Group I.

It is obvious that the bacillus of the cases forming Group II. differs sharply and clearly from the bacillus of the cases forming Group I., in that the former does not even in very large doses (50 mgrs. of culture) produce in the bovine body generalised progressive tuberculosis, while the latter does this always in these doses and may do it in much smaller doses.

Effects on Rabbits.

32. We have studied the effects of the injection, subcutaneously, intravenously, and intraperitoneally, of the bacillus of the cases of Group II. into rabbits, in the form both of emulsion and culture. Most of our results, however, have been obtained by the intraperitoneal injection of cultures in doses of 50 mgrs., 10 mgrs., 1 mgr., or 0·1 mgr. It will be sufficient to say that all the cases of Group II. agree in that, with certain exceptions (Viruses H. 50 "P.H.," H. 52 "T.F.," H. 33 "R.T.," H. 30 "E.M.," H. 9 "C.T.," H. 11 "E.D.," and H. 43 "F.F.") the injection of the bacillus into the body of the rabbit gives rise to a limited retrogressive tuberculosis only, and not to a fatal generalised progressive tuberculosis such as is produced by the like injection of the same dose, or even a much smaller dose, of the bacillus of bovine tuberculosis or of Group I.

Effects on other Animals.

Guinea-Pigs.

33. The bacillus of Group II. readily produces generalised progressive tuberculosis in these susceptible animals. As in the case of bovine tuberculosis and the tuberculosis of Group I. we have constantly made use of these animals for the purpose of continuing the virus and obtaining material for our experiments.

Pigs and Goats.

Our observations on the effect of injecting the bacillus of Group II. are not yet completed, but so far as they go they show that this bacillus is not able to produce generalised progressive tuberculosis in these animals, which appear to be as resistant as bovines and rabbits.

Monkeys.

Observations which we have made on these animals show that the injection of the bacillus of Group II. readily produces in them generalised progressive tuberculosis.

Anthropoid Apes.

We have obtained this result also with the anthropoid ape, namely, the champanzee.

FEEDING BOVINE ANIMALS WITH THE SPUTUM OF CASES OF HUMAN TUBERCULOSIS.

34. We chose, as material, the sputum of cases of phthisis, and fed for some considerable time two sets of animals with sputum of this kind obtained from a hospital. In the first experiment (H. 2. Sp. A.), we fed two heifers (not calves) with a daily dose of sputum, one for about 200, the other for about 300 days; each, therefore, must have received into the alimentary canal a very large number of bacilli.

In one heifer (11) several mesenteric and a few hepatic glands were found to be tuberculous, caseous, and calcareous; these were the sole tuberculous lesions present. We thus obtained by feeding with the bacillus present in human sputum a tuberculosis limited to the structures directly connected with the alimentary canal, a result similar to that which we obtained by feeding calves with the bacillus of bovine tuberculosis. The disease in Heifer 11 was, however, markedly retrogressive.

An emulsion (the number of bacilli present not being estimated) from these glands injected subcutaneously into a calf gave rise to a tuberculosis which, though general, and severe, was not fatal. Emulsions from various lymphatic glands of this second animal injected into six calves subcutaneously, intravenously, and intraperitoneally, gave rise to generalised progressive tuberculosis, fatal in the two injected intravenously, but not in the others within the 90 days which we have taken as our period of observation. Further, a culture derived from a guinea-pig injected with material of the tuberculous glands of Heifer 11, injected in dose of 50 mgrs., gave rise in two calves to fatal progressive tuberculosis, and to the same result when injected in a dose of 0·1 mgr. into a rabbit. We may add that a culture derived from one of the six calves mentioned above gave rise, in the smaller dose of 10 mgrs., to a fatal progressive tuberculosis in one calf, and to a generalised, but not fatal, tuberculosis in another. It is clear that the tuberculous glands in Heifer 11 contained a bacillus, possessing that degree of virulence which we have found to be characteristic of the bacillus of the cases in Group I. and of bovine tuberculosis. That bacillus must have been introduced by the sputum taken with the food; for in all our experience we have not met in our bovine animals at Blythwood any case of spontaneous tuberculosis of the mesenteric glands; and the animal gave no reaction to tuberculin before being fed with the sputum, though it did afterwards. Further, we may assume that the bacillus must have come from the tuberculous lesions of the patients expectorating the sputum; we cannot, for instance, admit as an explanation the suggestion that the bacillus in question might have come from milk supplied to the patients, the usual sterilisation of the milk having accidentally been omitted or having failed, and tubercle bacilli present in it having clung about the patient's mouth while he or she expectorated.

In the other heifer (13) tuberculosis of the mesenteric glands in the form of calcareous nodules, that is to say, in a stage of retrogression somewhat more advanced than the tuberculosis of Heifer 11 was found after death.

An emulsion from these calcareous glands, containing so few bacilli that none could be detected on microscopical observation, injected subcutaneously into a calf (111) gave rise to a very limited retrogressive tuberculosis, namely, to a small nodule in the prepectoral gland, the prescapular gland showing no visible tuberculosis, though an emulsion from it produced generalised tuberculosis in a guinea-pig.

That these limited results were not due to paucity of bacilli alone is shown by the fact that a culture derived from a guinea-pig infected with material from Calf 111, in a dose of 50 mgrs., produced in each of two calves not more than a limited retrogressive tuberculosis. We seem, therefore, by feeding to have introduced into the tissues of the bovine in the case of Heifer 11 a bacillus of the virulence of Group I., and in the case of Heifer 13 a bacillus of the virulence of Group II.

The history of these two cases is not without complications, but to these we refer later in § 58.

35. In a second experiment (H. 17, "Sp. B."), four calves were fed, one for 91, the other for 120 days, with sputum similar to that used in the first experiment, one receiving about 21,000 cc., the others about 30,000 cc. In each animal a limited retrogressive, calcareous tuberculosis was found in the mesenteric or adjoining glands; in some the pharyngeal glands were also affected. These results indicated the presence in these calves of a bacillus of the lesser virulence of Group II.

When from one of these calves we passed the virus on by injecting animals in succession, we obtained results of a different character; these we shall discuss later.

The Anatomical and Histological Features of the Tuberculosis set up by the Bacillus of Human Tuberculosis and by the Bacillus of Bovine Tuberculosis.

36. In each experiment which we have made the anatomical features of the disease set up has been carefully observed and recorded Under our direction Dr. Eastwood has also made a most careful and prolonged study of the histological features of the various lesions produced in the experiments. We have therefore abundant data for arriving at conclusions on these matters.

We may say at once that the effects of the bacillus of Group I. are, in respect to anatomical and histological features, absolutely identical with those of the bacillus of bovine tuberculosis. And this is true whether the effects on the bovine animal itself or on any other animal are studied. Further, the disease produced artificially in the bovine animal by the injection of, or feeding with, the bacillus of bovine tuberculosis, or that of Group I., is in every respect identical with the tuberculosis occurring naturally in that animal.

37. The effects on the bovine animal produced by the subcutaneous injection of the bacillus of Group II. present, on the other hand, a marked contrast to those produced by the bacillus of bovine tuberculosis. The limited circumscribed retrogressive local lesion, the limited retrogressive, or at least non-progressive, lesions in the adjacent lymphatic glands, the occasionally found, scanty, minute disseminate tubercles, in a distinctly retrogressive condition; all these features offer so strong a contrast to the usual effects of the bacillus of bovine tuberculosis as to suggest that the action of the one bacillus differs in kind from that of the other.

But, as we have seen (§ 5), in certain cases, owing to the smallness of the dose, or to the unusual resistance of the tissues of the animal employed, the effects produced by the bacillus of bovine tuberculosis fall short, to a varying extent, of what we have called (§ 4) the full effects, and in some of these cases the effects are, anatomically, identical with those of the bacillus of Group II., consisting as they do of a circumscribed retrogressive local lesion and scanty retrogressive disseminate tubercles. Histological investigation discloses, moreover, a like histological identity. The histological features of the disseminate tubercles produced by the bacillus of Group II. through the initial distribution spoken of in Section 29, are the same as those of the disseminate tubercles of like extent and phase produced by the bacillus of bovine tuberculosis. This is well brought out in cases Calf 185, H. 9, "C.T.," and Calf 365, H. 23, "J.P.," in which the amount of tuberculous disease set up by the initial distribution of the bacillus was unusually extensive.

The essential identity of the action of the bacillus of Group II. with that of the bacillus of bovine tuberculosis is further illustrated by the histological study of and initial changes following immediately upon subcutaneous injection and of the subsequent events in the two series.

In each of them the pathogenic processes resulting from the struggle between the bacillus and the tissue are fundamentally the same. The differences in the effects are determined by the relation of the virulence of the bacillus to the resistance of the tissues. The contrasts so marked between the two series are simply the qualitative expressions of quantitative differences of virulence. There is no evidence of difference in kind between the action of the one bacillus and that of the other.

The results which we obtained in the few instances in which we used intravenous inoculation were variable, but, so far as they go, they also afford no evidence of a difference in kind between the action of one bacillus and that of the other.

The above observations relate to tuberculosis set up in the bovine body, but they apply equally well to the tuberculosis set up in the body of the rabbit. We may add that in the exceptional cases referred to in § 32, in which the disease set up in the rabbit by the bacillus of Group II., though of slow course, was severe and progressive, the histological features were identical with those of the disease set up by the bacillus of bovine tuberculosis.

A much more ample opportunity, however, of comparing the anatomical and histological features of the tuberculosis set up by the bacillus of Group II. with those of the tuberculosis set up by the bacillus of bovine tuberculosis is afforded by the fact that both of them will set up generalised progressive tuberculosis in guinea-pigs and monkeys.

When we compare the broader anatomical features of the disease set up in the monkey by the bacillus of Group II. with those of the disease set up by the bacillus of bovine tuberculosis, we find no essential differences between the two, and that whether the bacillus be injected into the tissues or introduced by feeding through the alimentary canal. The progress of the invasion, the course of the pathological events, and the effects produced, are essentially the same. Nor has the most careful study of the more minute histological features of the lesions succeeded in disclosing any essential differences. The disease set up in the monkey by the bacillus of Group II. is essentially the same disease as that set up by the bacillus of bovine tuberculosis.

And what, in this respect, is true of the monkey, is also true of the guinea-pig. The tuberculosis set up in these animals is, so far as its anatomical and histological features are concerned, identical, whether it be set up by the bacillus of bovine source or the bacillus of Group I. or Group II. of human source.

Taking all these several facts into consideration, we feel justified in asserting that, regard being had to the differences which present themselves according to the extent of disease produced and the phase in which the disease exists at the time of examination, the tuberculosis set up by the bacillus of human source is, so far as its anatomical and histological features are concerned, one and the same as the tuberculosis set up by the bacillus of bovine source.

Summary of the Effects of the Bacillus of Tuberculosis.

38. We may sum up as follows the results of what in § 1 we put before us as our first task, namely, the study of the effects produced on animal bodies by the introduction of the bacillus of tuberculosis.

It is clear that the effects produced by the introduction of the bacillus from the cases of human tuberculosis forming Group I. are in every respect one and the same as the effects produced by the introduction of the bacillus of bovine tuberculosis.

But it is no less clear that the effects produced by the introduction of the bacillus of Group II. of cases of human tuberculosis are in one respect markedly different. The bacillus of Group II. is far less virulent than the bacillus of bovine tuberculosis; it is so much less virulent that, even in very large doses, it does not set up generalised progressive tuberculosis in the bodies of bovines and rabbits; when injected subcutaneously, its virulence is unable to overcome the "powers of resistance" of the tissues of these animals, and these powers either soon arrest the progress of any tuberculosis which may have begun, and make the disease retrogress or (in some few cases) prevent the disease being set up at all.

This difference is so pronounced, it affords so sharp a line of demarcation between the effects of the bacillus of Group II. and the effects of the bacillus of bovine tuberculosis, that we might be led to regard it as a difference in kind and to conclude that the former effects are not one and the same as the latter. Before we accept this conclusion, however, the following considerations deserve attention.

In the first place, it might be urged that the fact that a culture in a dose of 50 mgrs. produced generalised progressive tuberculosis in each of the cases of bovine tuberculosis examined by us (and in each of the cases of Group I.), but in none of the cases of Group II., does not justify us in concluding that the bacillus in each case of bovine tuberculosis (or of Group I.) possessed an equally high degree of virulence, and that the bacillus in each case of Group II. possessed an equally low degree of virulence. As we have said, we do not at present possess an adequate means of estimating small differences in virulence; it is possible that the bacilli in question do differ to a certain extent in virulence among themselves. If this be so, and if we were able to ascertain how far the most virulent bacillus of Group II. falls behind the least virulent bacillus of bovine tuberculosis, the result might show the difference between Group II. and bovine tuberculosis, though beyond doubt very great, to be not so great as is indicated by the results obtained with the subcutaneous injection of 50 mgrs. of culture. And, as will be seen later in § 53, in some of the cases in Group III. we have met with intermediate degrees of virulence.

In the second place, we have seen (§ 20) that the bacillus of bovine tuberculosis is virulent towards many animals other than bovines and rabbits, and, indeed, seems to be even more virulent towards some of these than towards the bovine animal itself. If it could be shown that the bacillus of Group II., in its effects on these other animals, instead of being less virulent, was as virulent as, or more virulent than, the bacillus of bovine tuberculosis, we might recognise this as indicating a difference in kind. But so far we have not yet met with such results. It must be admitted, however, that our observations on this point are at present scanty. Moreover, as we have already urged, the quantitative determination of virulence, especially when it is attempted to compare virulence towards one kind with virulence towards another kind of animal, is a task for which the methods at present at our disposal are very imperfect. Again, though we have seen that the pathological processes constituting tuberculosis are so far alike in most of the animals which we have studied (we are now confining ourselves to mammals) as to afford a basis for comparing the actions of different kinds of bacilli on different kinds of animals; yet there are exceptions to this general similarity. In the rat and the mouse, for instance, the pathological events of tuberculosis are strikingly different from what they are in the other animals of which we have made use. And this brings in new difficulties. Further, even in the animals in which the pathological processes are sufficiently alike to afford an adequate basis for comparison, it is obviously easier to estimate differences of virulence in a body susceptible to a certain degree to the action of the bacillus, but in which the powers of resistance are great, than in a very susceptible body in which these powers are very slight; the former affords a much wider range of observation than does the latter, in which a maximum effect is soon reached with even a small dose. We should not, for instance, expect to find a difference in virulence so readily in the guinea-pig and the monkey as in the bovine and the rabbit.

We repeat that our observations are not at present sufficiently numerous to justify us in making a decided statement; but so far as they go they seem to show that the bacillus of bovine tuberculosis is more virulent towards guinea-pigs and monkeys than the bacillus of Group II. And this, at all events, we are able to say, that in all our experience we have met with no instance in which the former bacillus has distinctly proved less virulent than the latter. We have come across no clear indication that the difference between the two is one of kind.

Lastly, if the difference which we are discussing be a difference in kind, we should expect to find it manifested by some differences not only in the amount but also in the character of the effects; we should expect to find, at all events, some differences in the anatomical, histological, and physiological features of the disease set up in the one case and the other. But, as we have shown in preceding paragraph, we have wholly failed to find any such differences; in all its essential features the disease set up by the bacillus of bovine tuberculosis is identical with that set up by the bacillus of Group II.; such differences as are met with are differences of amount and phase only.

With regard to the first part of our inquiry, then, that relating to the effects of the bacillus of bovine and human tuberculosis, we find that these are one and the same, save that those of Group II. of human tuberculosis are markedly less in degree.

All our results in fact point to the conclusion that the bacillus of bovine tuberculosis has sufficient virulence to produce easily its full effect on the more resistant bovine and rabbit as well as on other less resistant animals, while the bacillus of Group II. of human tuberculosis, being essentially less virulent, is not able to produce its full effect on the more resistant bovine and rabbit, though it can produce them on the less resistant guinea-pig, monkey, and, we may add, man.

We may now turn to the study of the properties and characters of the bacilli themselves.

THE TUBERCLE BACILLUS.

39. We have given in the Appendix full details of the procedures which we have adopted in our studies of the cultural and other characters of the tubercle bacillus. Each of our observers—Dr. L. Cobbett at

Blythwood and Dr. Griffith at Walpole—has prepared and studied cultures obtained from the tuberculous material made use of at the one establishment and at the other, that is to say, the original tuberculous material coming from the post-mortem room or the slaughter-house, and the tuberculous material afforded by our various experiments. In addition we assigned to Dr. Eastwood the task of carrying out in the laboratory at Royalcot an independent comparative study of the cultural characters of the bacilli from various sources sent to him in cultures from both Blythwood and Walpole. He was also instructed to observe, as well in the tissues sent to him for histological investigation as in the cultures which he prepared, the microscopic characters of the bacilli present.

It will be seen from the Appendix that our observers have made use of a large number of artificial media. They have employed serum obtained from different animals, glycerin-serum, that is, serum to which a small quantity (5 per cent.) of pure glycerin has been added, glycerin-broth, glycerin-agar, glycerin-potato, and other substances. Dr. Eastwood has made a special study of the influence of various substitutes for glycerin in broth cultures.

It is well known that when an attempt is made to grow the tubercle bacillus from this or that source on this or that medium great differences are met with in the rate at which the bacillus grows, the rapidity with which it multiplies, the way in which it spreads, and the kind of growth which it eventually builds up. Thus a bacillus taken from one source will grow, say, on glycerin broth, with very great difficulty, forming even after several weeks nothing more than a thin transparent film, while a bacillus from another source will grow on the same medium with great readiness, forming in very short time a thick, dense, often coloured crust. Bacilli from other sources may exhibit intermediate or other characters.

We have found it desirable to adopt some terms, to designate briefly the readiness or the difficulty with which a bacillus grows on a given medium; and we have adopted the words *dysgonic* and *eugonic* to denote respectively that the bacillus grows with difficulty or with readiness on a medium or on several media.

40. Dr. Eastwood has made use of several media, serum (chiefly ox and horse serum, but sometimes dog serum, and in a few instances pig serum), glycerin-broth, glycerin-agar, and glycerin-potato, for the purpose of differentiating bacilli in respect to their growth.

He finds that while bacilli from all sources grow, under proper conditions, equally well on serum, they exhibit marked differences when grown on the other media, especially gylcerin-agar. But for the purposes of differentiation he makes use of the behaviour of the bacilli, not as seen on one medium only, but on all the media used. Taking in this way the sum, as it were, of the growth on all these media, he finds that he can arrange all the bacilli which he has studied (that is to say, all the bacilli from various sources supplied to him, either in the original material from the post-mortem-room and the slaughter-house, or in the material furnished by some experiment), in a series, passing from the most dysgonic, or least luxuriant in growth, to the most eugonic, or most luxuriant in growth. He insists that this series is an unbroken one, the difference in growth between any two specimens adjoining each other in the series being almost an imperceptible one.

Nevertheless, he is able, by insisting on small differences, to divide the whole series into five Grades, Grade I. being the most dysgonic, and Grade V. the least dysgonic.

Dr. Cobbett, who was charged with the study of the bacillus of human tuberculosis, though making use of several media, has been led to trust largely to glycerin-serum as a convenient means of differentiation. He finds that, if care be taken to make use only of the cases in which the growth is in every respect satisfactory (whether it be luxuriant or the reverse), he can divide all the bacilli studied by him into two classes; those which will grow readily on glycerin-serum and those which will not. The former constitute a eugonic, the latter a dysgonic, class. He finds, however, that by the help of other media he can differentiate various members of each class.

Dr. Griffith, who was charged with the study of the bacillus of bovine tuberculosis, also making use of various media, finds, among other results, that the use of glycerin-serum enables him to arrange the bacilli present in the thirty viruses examined by him into three groups, according to their mode of growth. He also has observed smaller differences between the members of each group, so that the thirty viruses taken together present a series of gradually increasing luxuriance of growth. These results with glycerin-serum are confirmed by those with other glycerin media.

The results obtained by Dr. Cobbett and by Dr. Griffith agree, save for some very few and slight exceptions, with those obtained by Dr. Eastwood. The method adopted by the latter, however, enables us to differentiate the individual viruses more closely than does the simpler classification into two or three groups, and in what follows we have made use, mainly, of Dr. Eastwood's results.

The Bacillus of Bovine Tuberculosis.

41. *The Cultural Characters.*—The bacilli of the thirty bovine viruses examined by us do not agree as to the readiness with which they grow on artificial media. If we take, in the first instance, only the cultures obtained either direct from the original material or from the original material after a single passage through an animal body, generally that of a guinea-pig (and such a single passage we have not found to affect cultural characters), we find that a large number (nine in all) are very dysgonic and approximately equally dysgonic, being placed high up in Grade I., that four (IX. X. XI. XXIX.) are the least dysgonic, being placed in Grade III., and that the remainder are intermediate in character, Viruses V and XXV. being at the bottom of Grade II., that is to say close to Grade III. The bacilli, therefore, of bovine tuberculosis occurring naturally differ very considerably in their growth on artificial media. With some the growth on the three test media which we have employed is very scanty; with others the growth is much more abundant, the several viruses behaving in such a way that one passes in a most gradual manner, without any marked break, from the least to the most luxuriant, from the most to the least dysgonic.

A striking feature of the less dysgonic viruses is the irregularity of their growth; they exhibit a certain reluctance to grow, but not always the same reluctance; and they do not always grow in the same way; the same strain may, on different occasions, produce growths of very different characters. These less dysgonic viruses appear to be less stable in their cultural characters than the more dysgonic ones.

When in the case of a virus which grows with great difficulty on a glycerin medium, such as glycerin-serum, the scanty growth obtained at the first trial on this medium is replanted —on the same medium, the growth is found to be somewhat improved. By repeated "subculturing" in this way, the amount of growth on glycerin-media may be continually increased until full luxuriance is attained. Indeed, in the end, all viruses differing so much to start with may, with some few exceptions, be brought to grow on glycerin-media with equal luxuriance. Moreover, a culture thus improved in growth may be passed through an animal body without losing the improvement thus gained.

We have had several opportunities of studying the cultures of some of these thirty viruses after the virus had been passed experimentally through the body of a bovine or other animal, or through several bodies in succession. In most cases no change in the characters of the culture has been observed; again and again, for instance, a virus has been passed through even a succession of guinea-pigs without any change whatever being brought about. In other cases some change has been observed. If Dr. Eastwood's list be examined, it will be seen that the several cultures belonging to Virus I. and Virus IV. occupy somewhat different positions in the list; in some of these instances the culture after the passage through another animal body is less dysgonic, in others more dysgonic, than the culture from the original material. In most instances the changes have been slight, and no importance can be attached to them; but in one instance, which has been confirmed by Dr. Griffith, Baboon 8, Virus I., the change has been more marked, viz., from Grade I. to Grade III.

Our observations on these changes in cultural characters are at present too few to enable us to draw very definite conclusions, but are being continued. This however at least is clear, that the physiological processes which determine the growth of the bacillus on artificial media, whatever be the exact nature of those processes (and our knowledge concerning them is as yet most imperfect), are such that the cultural characters do not remain absolutely fixed and constant, but are subject to change, and a change may at times be brought about by passing the bacillus through an animal body.

42. *Microscopical Features.*—The bacillus of tuberculosis is a very minute, colourless, almost transparent organism, very simple in structure. Even using the best methods of microscopical inquiry we are able to note little more than its length and relative breadth, whether it is straight or curved, and whether when subjected to the appropriate staining reagents it stains uniformly, or intermittently along its length so as to appear "beaded."

Examined in the animal tissues in which they have grown the bacilli of bovine tuberculosis are found to be very variable in every respect and to present many irregularities. They vary in length from $6{\cdot}5\mu$* (or more) to about $0{\cdot}5\mu$ with a mean varying in the several tissues from $3{\cdot}3\mu$ to $1{\cdot}26\mu$. The percentage of those which are straight varies in the several instances from 94 to 46, and of those which are uniformly stained from 90 to 22.

Grown on serum, horse serum for instance, they are much more uniform. Their average length is 1μ or a little less; they are often all straight and all uniformly stained, and the percentage never falls in either respect so low as 90. The bacillus of bovine tuberculosis grown on serum may be briefly described as short, straight, and uniformly stained.

Grown on other media, the bacilli are found to be more irregular in all these features, and that, broadly speaking, in proportion to the luxuriance of the growth. On all the three media the bacilli of Grades II. and III. present greater and more numerous irregularities than do the bacilli of Grade I.

In this irregularity of its scanty microscopical features when grown on various media, and in the relation of its variations to the luxuriance of growth, the bacillus of bovine tuberculosis resembles other similar organisms of a like simple structure.

The Bacillus of Human Tuberculosis.

It will be desirable to consider Group I. separately from Group II.

GROUP I.

43. *Cultural Characters.*—We may say at once that the cultural characters of the bacillus of this group are in every respect identical with those of the bacillus of bovine tuberculosis. In all cases the bacillus may be described as dysgonic, though to a varying degree in the several cases, and the range of variation coincides almost exactly with the range of variation shown by the bacillus of bovine tuberculosis. In one case (H. 28 "C.L.") the bacillus is as dysgonic as the most dysgonic of the bovine bacilli, being placed in Grade I.; the least dysgonic (H. 19 "S.W.", H. 32 "Y.W.", and H. 7 "C.M.") are placed in the same position in Grade III. as the least dysgonic of the bovine bacilli, namely, B. IX., X., XI. Dr. Cobbett's results, obtained, as explained in § 40, coincide with those of Dr. Eastwood. For though he divides all the cases into two classes only, dysgonic and eugonic, he places all the cases of this group in his dysgonic section with the exception of H. 7 "C.M." which Dr. Eastwood also finds to be the least dysgonic of all the group.

To the above bacilli obtained from cases of human tuberculosis we may now add the bacillus obtained from (H. 2, "Sp. A.") Heifer 11 by feeding with human sputum and which was we found (§ 34) to possess the greater virulence characteristic of Group I. and of bovine tuberculosis. In cultural characters also this bacillus agrees with those of Group I. but with the least dysgonic members of the group. It is placed in Grade III. and one strain, that from Guinea-pig 690, occupies a place by itself at the bottom of the grade; this position is not inconsistent with the description of the bacillus by Dr. Cobbett as being eugonic.

44. *Microscopical Features.*—It will be sufficient to say that the microscopical features of the bacillus of Group I. are, in all respects, the same as those of the bacillus of bovine tuberculosis. Growing in animal tissues they

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* $\mu = {\cdot}001$ millimetre.

exhibit a similar range of variation in their several features, grown on serum they exhibit the like greater uniformity, and grown on other media they exhibit a like relation of variation in structural features to luxuriance of growth.

If, for instance, we compare the descriptions of the features of the bacilli grown on horse serum of H. 28 "C.L." and of B. I. or B. III., taking these typical of the most dysgonic of the bacilli of Group I. and of bovine tuberculosis, we find them almost identical. Taking also the descriptions of the two sets of bacilli as grown on broth, we again find them almost identical.

If we compare, similarly, the descriptions of the bacilli of H. 38 Y.W. and B. XI., taking these as characteristically least dysgonic forms, we find again a similar identity, both when the bacilli are grown on horse serum and when they are grown on broth. A similar likeness holds good in the case of all the viruses for all the various grades of dysgony observed with the various media used.

GROUP II.

45. *Cultural Characters.*—With this group the results are different. The cultural characters of the bacillus in all the members of this group are different from those of the bacillus of Group I. and of bovine tuberculosis. The several cases exhibit great variations in the cultural characters of the bacillus; but the variations fall within Grades IV. and V., with one exception (viz : H. 58 "F.G.") which falls in Grade III., which contain no representative of Group I. or of bovine tuberculosis (excluding the exceptional instances of Dogs 18 and 50); and by Dr. Cobbet's method they are all found to be eugonic. Their range of variation is a wholly different one from the range of variation seen in Group I. and in bovine tuberculosis. It will be remembered that Group II. does not include certain cases, exceptional cases, which we shall have to consider later. These exceptional cases are, however, included in Dr. Eastwood's list.

46. *Microscopical Features.*—When growing in animal tissues the bacilli show, in their structural features, great variations, similar to those seen in the bacilli of Group I. and of bovine tuberculosis; the two are in this respect alike.

When grown on serum the bacilli are found to be straight, uniformly stained, and with a length varying from $0{\cdot}5\mu$ to $1{\cdot}5\mu$ or 2μ; that is to say they resemble, in this respect, the bacilli of Group I. and of bovine tuberculosis, with which they agree in their mode of growth on serum. And this is true both of those growing less readily (Grade IV.) and of those growing more readily (Grade V.) on other media.

When the bacilli growing on other media are examined, and are compared with the bacilli of bovine tuberculosis, they are found to be, on the whole, longer, and especially to vary more in length, to be less regularly straight, and less uniformly stained. The extent of irregularity is, broadly speaking, proportionate to the luxuriance of growth. Since these bacilli all grow more luxuriantly on these media than do the bacilli of Group I. and of bovine tuberculosis, they present on these media a difference, and often a very marked difference, from these bacilli.

A Special Physiological Reaction.

47 When the bacillus of tuberculosis is growing on an artificial medium it necessarily, through the processes of its growth, brings about chemical changes in the medium. These are presumably very complex, and are at present very little understood; we are ourselves carrying on some inquiries as to the nature of these changes, but are unable to make any definite statement at present.

When the bacillus of tuberculosis is grown on glycerin broth of known (slight) alkalinity, and the reaction of the medium carefully estimated from time to time as growth proceeds, it has been observed that in some cases the reaction of the medium increases slowly in alkalinity, and the increase continues so long as growth is observed, while in other cases an initial increase of alkalinity is succeeded, after a while, by the reversal of the reaction, the medium becoming acid and increasing in acidity as growth proceeds. The former behaviour is shown by the bacillus of bovine tuberculosis, the latter by the bacillus of Group II. of human tuberculosis. This result seems to establish a physiological difference of specific value between the two cases.

We have repeated these observations with great care and can confirm the general result. But we find that the development of acidity in the medium is so directly correlated with the amount of growth as to leave little doubt but that the reason why the acidity does not appear in the broth culture of bovine tuberculosis and does appear in the broth culture of Group II. of human tuberculosis is simply because the growth of the bacillus is so much more luxuriant in the latter than in the former. We find moreover that the continuation of alkalinity is less marked in the more luxuriantly growing cultures than in the less luxuriantly growing cultures of bovine tuberculosis. So that the character loses its special significance; it is merely a striking indication of luxuriance of growth, and we cannot deduce from it more than we can from the luxuriance of growth itself.

Summary of the Characters of the Bacillus of Tuberculosis.

48. The bacillus of tuberculosis is a simple organism with scanty microscopical features, growing with varying ease or difficulty on various media. The microscopical features of the bacillus itself and the changes which it brings about in the medium on which it is growing are correlated to, and seem dependent on, the nutritive powers of the bacillus; in this respect the bacillus of tuberculosis resembles other similar simple organisms. This difference in nutritive and so in reproductive power is the essential difference between one bacillus of tuberculosis and another, the other differences described above being dependent on it; and this difference enables us to arrange all the bacilli which we have studied into two classes; one in which the bacillus grows with difficulty on artificial media and which we call dysgonic, and another in which the bacillus grows readily on the same media and which we call eugonic.

In the first class we place the bacillus of bovine tuberculosis and the bacillus of Group I. of human tuberculosis. These exhibit the same range of growth on various media and the same correlated variations in microscopical features. They are in all respects one and the same.

In the second class we place the bacillus of Group II. of human tuberculosis.

But the demarcation between these two classes is not a sharp, or broad one. The members of the former class are not equally dysgonic, nor are those of the latter equally eugonic. In each of them there is a wide range of growth, so wide in each class that the least dysgonic of the former differs slightly if at all from the least eugonic of the latter class. And there is a similar closeness in the other features correlated to the power of growth.

Hence the difference between the two classes, that is between the bacillus of Group II. of human tuberculosis and the bacillus of bovine tuberculosis (or of Group I. of human tuberculosis) is one of degree only, and, moreover, when the extremes of the two classes are compared the one with the other, is seen to be a slight one.

BOVINE AND HUMAN TUBERCULOSIS COMPARED.

49. We are now in a position to attempt a direct answer to the question, are human and bovine tuberculosis one and the same?

It is obvious, however, from what has gone before that in attempting the answer we must deal separately with the human tuberculosis of Group I. and that of Group II.

Group I.

The results relating to this Group, recorded in foregoing paragraphs, show beyond all doubt that the tuberculosis occurring in the cases forming this Group cannot, either by the effects brought about when the bacillus is introduced into the bodies of bovine or of other animals, or by the cultural and other characters of the bacillus itself, or indeed in any other way, be distinguished from bovine tuberculosis, that is to say, from tuberculosis occurring naturally in the bovine animal. We may go a step further.

The tuberculous material of Group I. was supplied to us in the form of mesenteric or cervical glands; and when the details of the several cases are studied, it seems clear that the bacillus found an entrance into the body by way of the alimentary canal, through absorption from the fauces (cervical glands) or from the intestines (mesenteric glands).

Now, the spread of tuberculosis from man to man is generally held to take place mainly through the respiratory passages. The bacillus is thrown off from the body of man mainly with the sputum, and through the sputum gains access to the human body chiefly in the inspired air, by the channel of the respiratory passages. Some of these air-borne bacilli may, it is true, be absorbed from the fauces before they can reach the respiratory passages proper; and bacilli of human source may in various ways contaminate human food, and be absorbed from the intestine; but it is generally considered that the amount of infection which takes place by these means is not great.

Very different are the conditions determining the entrance into the human body of bacilli coming from a bovine source. The opportunities for the transmission to the body of man by the respiratory passages of the air-borne bacilli coming from the lungs of a tuberculous cow are insignificant compared with the abundant opportunities for the transmission to man, by the fauces or by the intestines, of tubercle bacilli present in cows' milk. We are therefore led to a conclusion from which there seems to be no escape, not only that the tuberculosis which was present in each of the cases of Group I. was identical in all its features with bovine tuberculosis, but also that the bacilli actually came from a bovine animal; the tuberculosis was bovine tuberculosis implanted in a human body.

In the three cases in which the materials studied by us consisted of cervical glands removed by operation, there was no evidence of disease in any other part of the body; and in the case in which the material consisted of a cervical gland taken from a child dying of abdominal tuberculosis, we received the cervical gland only, and can say nothing about the abdominal lesions.

In three of the cases in which we obtained tuberculous mesenteric glands, we were able to study not only the mesenteric glands themselves, but also tuberculous lungs and other organs; and the results obtained from these other tuberculous organs were identical with the results obtained from the mesenteric glands; the tuberculosis in all the affected organs was the same bovine tuberculosis, one form only of bacillus having been found. The bacilli of bovine source had not only attacked the mesenteric glands to which they had been brought directly by absorption from the alimentary canal, but had also invaded distant organs, being carried thither by the blood stream or the lymphatics. We may conclude beyond doubt that the whole disease was caused by the same bovine tubercle bacilli; the children died of bovine tuberculosis caused by bacilli introduced by way of the alimentary canal, and probably conveyed through cows' milk.

In each of the other cases we have been able to study the nature of the tuberculosis in the mesenteric glands only. We are unable to make any positive statements as to the nature of the tuberculosis in the other diseased organs. But in our study of these other cases we have met with no facts which would prevent us drawing the conclusion that these cases, inasmuch as they agree with the above three cases in all respects in which we have studied them, agree also in this, that the whole disease was caused by a bacillus coming from a bovine source.

We are thus able to give a positive answer to the second term of our reference. The human body can be infected by bovine tuberculosis. Moreover, the results which we have recorded in preceding paragraphs show that the bovine body can be infected by tuberculosis of human source, in some cases to a complete, in others to a limited extent; bovine animals and man can be reciprocally infected.

But, it may be urged, we have not shown that human and bovine tuberculosis are one and the same. All that we have shown by the study of the cases of Group I. is that some cases which are called cases of human tuberculosis are in reality cases of bovine tuberculosis. We must now turn to the other group.

Group II.

50. We have seen (§ 37) that a most marked difference in "virulence" obtains between Group II. and Group I.; even in very large doses the bacillus of Group II. does not set up generalised progressive tuberculosis in the bovine animal. But we have also seen that this difference, great as it appears to be, is a difference of degree only; for the pathological changes (§ 36) which constitute the disease called tuberculosis can be set up to a certain extent in the bovine tissues by the bacillus of Group II. The changes brought about by the bacillus of Group II. and by the bacillus of Group I. are, at the outset of their respective actions, one and the same; it is in the sequent changes that the difference is manifested; apparently the weaker bacillus of Group II. is soon overcome by the resistance of the tissues, while the stronger bacillus of Group I. goes on to bring about the further changes constituting progressive tuberculosis.

We have also seen (§ 47) that the bacillus of Group II. differs from that of Group I. in the properties which we sum up under the term "cultural characters." In all the cases of Group II. the bacillus grows on artificial media more readily than does the bacillus of Group I. We may perhaps speak of the bacillus in all the cases of Group I. as being (more or less) dysgonic and of the bacillus in all the cases of Group II. as being less or more eugonic.

But while the difference in virulence between Group I. and Group II. is a very marked one, creating a broad gap between the two, the difference in cultural characters is, so to speak, a vanishing one. The bacilli of the several cases of Group I. differ widely among themselves as to the readiness with which they grow on artificial media, as do also and almost equally the bacilli of the cases of Group II., so that the difference between the least dysgonic of Group I. and the least eugonic of Group II. is almost an imperceptible one. The connection between virulence on the one hand, and readiness to grow on artificial media on the other hand, is obviously a very complex one, liable to be modified by various contingencies. It seems clear that in a broad way "virulence" and the power to multiply on artificial media stand in an inverse relation to each other; the more virulent bacillus of tuberculosis grows with greater difficulty on artificial media than does the less virulent one; but there is no consistent parallelism between the one property and the other. We have been unable so far to find any differences corresponding to the cultural differences in virulence between the more dysgonic bacilli of Group I. placed in Grade I. and the less dysgonic placed in Grade III., or between the less eugonic bacilli of Group II. placed in Grade IV. and the more eugonic placed in Grade V.

Notwithstanding this want of parallelism we have before us the broad fact that the bacillus of Group II., the more common bacillus of tuberculosis in man, differs from the bacillus of Group I. and the bacillus of bovine tuberculosis, not only in being very much less virulent, but also in the way in which the two respectively grow on artificial media. The difference in virulence is confirmed by the difference in cultural characters. The agents are unlike, and they act in unlike ways.

In the face of this twofold difference it might seem impossible at first sight to assert that the human tuberculosis of Group II. is one and the same as bovine tuberculosis.

51. Before, however, we accept the conclusion that the two are not one and the same certain aspects of the problem before us have to be considered.

It is a matter of common bacteriological, or rather biological, experience that simple micro-organisms, similar to the bacillus of tuberculosis, when growing either in living tissues or on artificial media may in certain cases be so influenced by their environment that, after a longer or shorter time, their characters and properties are changed. Pathogenic organisms may in this way lose or gain in virulence. Bacteriological experience furnishes us with many examples of a pathogenic organism being lowered or raised in virulence, and at the same time modified in its other characters, by being cultivated in the living tissues of this or that animal, that is to say, by being "passed" through the body of this or that animal. In such cases the organism remains "one and the same," but it is changed in virulence and often in other characters.

Now, compared with many other pathogenic micro-organisms the bacillus of tuberculosis (whether of human or bovine source) is a very stable organism;

it does not so readily exhibit changes in its characters as do many other pathogenic micro-organisms. Our own experience has given us many instances of this stability. We have, again and again, had occasion to "pass" a virus through a considerable number of animal bodies and to observe that it was not thereby changed either in virulence or in cultural characters. Again we have, by repeated "sub-culturing" often maintained a virus in the form of a culture for a long time, for many months, and found that it was not modified by cultivation either in virulence or cultural characters. But this stability, though great, may not be absolute, and we are thus led to the question, May the bacillus of bovine tuberculosis on the one hand, and the bacillus of human tuberculosis on the other hand, exhibit instability under certain conditions?

May, for instance, the bacillus of bovine tuberculosis be so subjected to the influences of some environment as to be modified in its properties, to lose in virulence and to gain greater power to grow on artificial media? May the bacillus of human tuberculosis be similarly modified so as to gain in virulence, and lose its so-called "saprophytic" power, its power to grow on artificial media? In other words, may the bacillus of bovine tuberculosis by cultivation in living tissues, by "passage" through some animal body or bodies, or in other ways be transformed into the bacillus of human tuberculosis, and *vice versâ*?

These questions bring us to the consideration of the cases of tuberculosis in man yielding exceptional results which we have placed in a group by themselves, Group III.

CONSIDERATION OF THE CASES FORMING GROUP III.

52. We have placed these case in a Group, but they do not form a Group in the sense in which the cases of Group I. and of Group II. form a Group. In Group I. and Group II. the cases in each Group differ so little from each other as to form an almost homogeneous Group; in Group III. the cases differ widely from each other; we simply group them together for consideration on account of their exceptional features. Were it not for these exceptional features, some might be placed in Group I., others in Group II.

Case H. 53. "D.H." was a case of that special form of human tuberculosis known as Lupus. Scrapings from the affected skin were injected into a guinea pig, and from the diseased organ of this animal a culture was obtained.

Of this culture (8 months old) 50 mgrs. injected into a calf (905) gave rise to a tuberculosis, generalised but not severe, and not fatal within the period of observation. Later on 50 mgrs. of the same culture ($14\frac{1}{2}$ months old) injected into each of two calves gave rise in each to nothing more than a limited retrogressive tuberculosis. A culture obtained from the tuberculous prescapular gland of the calf first employed (905) and used when quite fresh, when injected in a dose of 50 mgrs. into each of two calves gave rise in one to a generalised progressive tuberculosis, not fatal, however, within the period of observation, and in the other to an exceedingly limited retrogressive tuberculosis. Injected in a dose of 10 mgrs. into each of two calves, the same culture gave rise in one calf to a generalised tuberculosis, not fatal within the period of observation and indeed not severe, and in the other to a limited retrogressive tuberculosis. These results seem to show that the bacillus of this case was intermediate in virulence; its virulence was greater than that of Group II. but distinctly less than that of Group I. The cultural characters to a certain extent correspond. The culture from the guinea pig is placed by Dr. Eastwood in his Grade III., on a level with Viruses B. IX., B. X., and B. XI.; the culture from Calf 905 is placed by him also in Grade III., but on a lower level.

It is worthy of notice that the cultures obtained from this case though distinctly falling below those of Group I. (and bovine tuberculosis) in virulence towards calves, were virulent for rabbits, producing fatal generalised tuberculosis in so small a dose as 0·01 mgr. This is the only case we have hitherto met with in which a bacillus shows a marked difference in its virulence towards calves from that towards rabbits.

53. Case H. 49 "T.C." was a case of a lad (æt. 18) with tuberculous disease, primary in the abdomen, but extending to the thorax. A culture was obtained directly from the mesenteric glands; the attempt to obtain a culture from the lungs failed.

The culture (two months old) in a dose of 50 mgrs. gave rise to fatal generalised progressive tuberculosis in one calf (787) and to a limited retrogressive tuberculosis in another (797). It gave rise to fatal generalised progressive tuberculosis in rabbits, in even so small a dose as 0·01 mgr. The same culture (7 months old), when injected in a dose of 50 mgrs. into each of two calves, gave rise in each to a fatal generalised progressive tuberculosis; when injected in a dose of 10 mgrs. into each of two calves the same culture gave rise in one calf to a generalised progressive tuberculosis fatal in 108 days, and in the other to a generalised tuberculosis not severe and not fatal within the period of observation. A culture obtained from the prescapular gland of Calf 797 (in which the original culture had produced only a limited retrogressive tuberculosis), used as a first subculture, the strain being two months old, produced fatal generalised tuberculosis in two calves both in a dose of 50 mgrs. and also in a dose of 10 mgrs.; it also produced a rapidly fatal generalised progressive tuberculosis in rabbits even in so small a dose as 0·01 mgr.

The original culture thus exhibited a virulence somewhat below that of Group I.; this is especially shown by the duration of life after the injection; but the second culture, that from Calf 797, exhibited full virulence. The original culture and the culture from Calf 797 are placed by Dr. Eastwood in about the middle of his Grade II.

The case therefore presents in the first place a virulence tending to be intermediate between the standard of Group I. and that of Group II., and in the second place a change in, an increase of, virulence in passing through the body of Calf 797. Further the original culture when used in the 7th subculture (always on serum), the strain being 9 months old, failed to produce generalised tuberculosis in rabbits, and when used in the 14th subculture, the strain being 14 months old, failed to produce generalised tuberculosis in rabbits, even in a dose of 10 mgrs., and injected into a calf in a dose of 50 mgrs. produced only a very limited retrogressive tuberculosis.

Now, in respect to the bacilli of bovine tuberculosis and the bacilli of Group I., we have carried out many experiments to ascertain whether or no virulence is diminished by repeated subculturing. We have in no case observed any such diminution. Such a diminution as is shown by the present case may be taken, in the absence of any other explanation, as evidence of instability. Hence the virus of H. 49 "T.C." shows a virulence not only intermediate but also unstable, its virulence appearing to be diminished by cultivation on an artificial medium and to be increased by passage through a bovine body.

Passage Experiments.

54. We have placed in this Group III. three cases in which we obtained certain results when the virus was "passed" through a series of calves in succession. We have placed them in this Group for this reason only; but for this they would have been placed in Group II. We will briefly describe the "passage" experiment in each case.

In one case, H. 16 "J.H.," the tuberculous material, namely, tuberculous synovial membrane removed from the knee joint of an adult, when injected subcutaneously into two calves gave rise to a limited retrogressive tuberculosis. A culture obtained from the affected organs of one of these two calves (Calf 157) was very distinctly eugonic, being placed in Grade V.; and a culture, obtained from the organs of a guinea-pig inoculated with the original material, when injected subcutaneously into calves in a dose of 50 mgrs., and intraperitoneally into rabbits in a dose of 10 mgrs., gave rise to a limited retrogressive tuberculosis. The bacillus of this case clearly belonged to Group II.

When, however, this material was passed in succession by subcutaneous injection through a series of calves, emulsions of the organs of the animals of the fifth and sixth passages gave rise to a generalised progressive tuberculosis, and cultures obtained from these organs gave rise in calves and in rabbits to fatal progressive tuberculosis. These cultures, moreover, were highly dysgonic. One of them, indeed (that of Calf 423a), was one of the most dysgonic obtained by us from a human source. The bacillus, then, present in the organs of these calves, infected after a number of "passages," presented all the characters of the bacillus of bovine tuberculosis.

55. In another case, H. 13 "A.D.," tuberculous material obtained from the bronchial glands and spleen of a child (æt. 4) who died of acute generalised tuberculosis gave rise in each of two calves, after subcutaneous injections, to a very limited retrogressive tuberculosis, the glands nearest to the seat of injection being the only parts obviously infected. Unfortunately, we obtained no cultures from the original material or from either of the two calves; we are therefore unable to make any exact statement of the properties of the bacillus in these. But a culture from the organs of a calf (Calf 301) rendered tuberculous by the subcutaneous injection of material derived from one of the above two calves after passage through three guinea-pigs in succession, gave rise in a dose of 50 mgrs. in one calf to a very limited tuberculosis, and in another to a more generalised tuberculosis, which, however, did not seem to affect the health of the animal. Injected intraperitoneally into a rabbit in 1 mgr. dose and even in so large a dose as 50 mgrs., it gave rise to not more than a limited retrogressive tuberculosis. The culture was eugonic but only moderately so, being placed in Grade IV. The bacillus present in Calf 301 possessed the characters of the bacillus of Group II.; it was not, however, quite typical of this group.

Emulsions from the organs of Calf 301, on subcutaneous injection in adequate doses into calves, gave rise to generalised progressive tuberculosis, and a culture obtained from the organs of one of these, Calf 321, injected subcutaneously into calves in 50 mgr. doses, and intraperitoneally into rabbits in 1 mgr. doses, caused fatal generalised progressive tuberculosis. The culture, moreover, was extremely dysgonic, being placed with the culture of H. 16 mentioned above in Grade I. In fact it, with a culture obtained by passage through a rat from Calf 301, actually heads the list drawn up by Dr. Eastwood.

In this case, again, though the bacillus of the original material possessed, we may conclude, the characters of a bacillus of Group II., the bacillus cultivated after passage, in this case a short one, possessed the characters of the bacillus of bovine tuberculosis.

56. We also carried out a "passage" experiment with the bacillus of the tuberculous lesions produced in a calf by feeding with human sputum: H. 17, "Sp. B."

It will be seen by referring to § 35 that the results obtained showed, in the tuberculosis set up in each of the four calves by feeding with human sputum, the presence of a bacillus having the lesser virulence of Group II. We can now add that the bacillus of a culture obtained from one of the four calves, namely, Calf 161 (through Calf 265), was extremely eugonic, being placed in Grade V.

The tuberculous material of another of the four calves (Calf 169), after passing through two guinea-pigs was injected subcutaneously, in the form of an emulsion into a calf (Calf 339). It produced a limited retrogressive tuberculosis; and a culture from the tuberculous organs of this calf (through a guinea-pig) was very eugonic, and gave rise in calves in a dose of 50 mgrs., and in rabbits in a dose of even 50 mgrs. to not more than a limited retrogressive tuberculosis. Clearly the bacillus of the tuberculosis of this Calf 339 possessed the characters of a bacillus of Group II.

The tuberculous material of Calf 339 was injected in the form of an emulsion, not subcutaneously but intravenously into a second calf, and from this in succession, in each case intravenously, in the form of an emulsion into a third, fourth, and fifth calf.

An emulsion from the tuberculous organs of the fifth calf (Calf 553), injected subcutaneously in a dose of 150 million bacilli into each of two calves, gave rise in each to a fatal generalised progressive tuberculosis. A culture derived from one of these two calves (Calf 555) was extremely dysgonic, being placed in Grade I.; and a culture from Calf 553 itself (through a guinea-pig) gave rise in calves in even a dose of 10 mgrs., and in rabbits in a dose of 0·1 mgr. to a fatal generalised progressive tuberculosis.

In this case, again, the bacillus obtained after passage possessed the characters of the bacillus of bovine tuberculosis.

57. Thus in each of these three cases the bacillus of the tuberculous materials made use of either actually presented, or may be assumed to have possessed, at the beginning, the characters of a bacillus of Group II., highly eugonic and of lower virulence; but, after "passage" through bovine bodies,

presented the characters of a bacillus of bovine tuberculosis highly dysgonic and very virulent.

We have attempted to repeat these "passage" experiments, making use of two of the three cases described above and also of four cases from Group II., but beginning with a culture not an emulsion. The result was in each case negative; but in none of them can the experiment, for one reason or other, as may be seen from the details given in the Appendix, be regarded as adequately parallel to the three experiments in question.

We have also carried out "passage" experiments with rabbits, passing the material of eleven cases (one of them H. 16 "J. H.") intravenously or intraperitoneally through the bodies of rabbits, making two, three, or four or even more passages in each case. So far the results have been negative.

The negative result obtained in all the above experiments, even admitting that they were not wholly satisfactory, at least shows that the change in the characters and properties of the bacillus witnessed in the three passage experiments under discussion is not an invariable result of passage. We may safely assume that in the three experiments in question certain special conditions were present, and these special conditions determined that during the passage the initial eugonic bacillus of low virulence was in some way or other replaced by the final dysgonic bacillus of high virulence.

Instability.

58. Before proceeding further it will be convenient to make a brief statement of certain results bearing on the stability of the tubercle bacillus which we have met with in the course of our investigations.

We find that the cultural characters are not absolutely stable. Dysgonic bacilli which grow with difficulty on glycerin serum or glycerin broth may by repeated sub-culturing on such a medium be finally induced to grow with ease upon it. The bacilli of Grade III., whether of bovine or human source, have been observed by Dr. Eastwood to be irregular and uncertain in their growth on glycerin media; samples taken from the same culture on serum will grow on glycerin broth and other glycerin media in different ways, presenting different kinds of growth.

In respect to stability in virulence which is not necessarily affected by cultivation, for we have repeatedly kept a strain for a long time (in one instance three years) in cultivation without any lessening of virulence, the following results deserve attention:—

In H. 16, "J.H.," one of the "passage" experiments, an emulsion from the greatly diseased prescapular gland of Calf 273, affected with a generalised though not fatal tuberculosis, proved to be highly virulent, producing fatal generalised progressive tuberculosis in the calf and in the rabbit. Yet a culture from this gland, after having been sub-cultured for six generations, being ten months old, did not possess the virulence indicated by the emulsion; it exhibited the low virulence of Group II., and moreover it was very eugonic, being placed in Grade V., side by side with a culture from Calf 157, injected with the original material.

In H. 13, "A.D.," also a passage experiment, the long thoracic lymphatic gland of Calf 301, affected with a fatal generalised progressive tuberculosis, gave a highly virulent emulsion, causing fatal generalised progressive tuberculosis in the calf and the rabbit. Yet a culture from this gland injected in a dose of 50 mgrs. failed to produce this result; it had not the virulence of the emulsion, and moreover, when examined in the third sub-culture was found to be moderately eugonic, being placed in Grade IV.

Again in the first feeding experiment, H. 2, "Sp. A.," the emulsion from the affected glands of Heifer 13 did not always show the same virulence. Injected into Calf 111, it gave rise only to an exceedingly limited retrogressive tuberculosis, and a culture obtained through a guinea-pig from the affected organs of this calf also possessed a very low virulence. Yet the same emulsion "passed" through a guinea-pig (the effect of which, as we have seen again and again, is only to increase the number of bacilli, not in any way to change their character) and injected into Calf 153 produced a fatal generalised progressive tuberculosis, so severe that it is impossible to attribute the result to any special susceptibility of the animal.

We are, however, continuing our observations on these apparent instances of instability.

We may also, in this connection, call attention to some striking instances of want of accordance between cultural characters and virulence. The culture from the just mentioned Calf 111, though of low virulence, was dysgonic, being placed in Grade III. very close to the culture from Calf 93, H. 2, "Sp. A.," which possessed the high virulence of Group I. It should be noted, however, that the cultures from the experiments of feeding with sputum were irregular in their growth, so that it was difficult to define exactly the cultural characters of the bacillus.

Again, the culture from Rabbit 181 (H. 17, "Sp. B."), though highly virulent, was distinctly eugonic, being placed in Grade IV.

Further, all the bacilli, whether of bovine or human source, placed in Grade III. present this feature, that while distinctly less dysgonic than the bacilli placed in Grade I. (and, though of course to a less extent, than those placed in Grade II.) they appear to be quite as virulent as those of Grades I. and II.

59. In the cases then which we have put together in Group III., and in the cases of feeding with human sputum, we have met with the following :—

(*a*) Bacilli of a character intermediate between Group I. and Group II. (H. 53, "D.H.," H. 49, "T.C.").

(*b*) Replacement of a eugonic bacillus of low virulence by a dysgonic bacillus of high virulence. ("Passage" experiments H. 16 "J.H.," H. 13 "A.D.," H. 17 "Sp. B.")

(*c*) Indications of instability in virulence and cultural characters, and of want of accordance between virulence and cultural characters.

Two possible Explanations of the Cases of Group III.

60. When we attempt to reconcile the results obtained in the passage experiments and in the other cases of Group III. with the results obtained in the cases of Group I. and Group II., two explanations may be put forward.

On the one hand we may suppose, in respect to the "passage" experiments, that H. 16, "J.H.," and H. 13, "A.D.," and Calf 169, H. 17, "Sp. B.," were in some way or other infected both with bacilli of human source, and also, though to a much less extent, with bacilli of bovine source, and that hence, in each case, the original material contained bacilli of human source, possessing the characters of Group II. (which, for brevity's sake, we may speak of as bacilli of human tuberculosis), mixed with so small a number of bacilli of bovine tuberculosis that the emulsions, and cultures, of the original material behaved as if they contained bacilli of human tuberculosis only, exhibiting a low virulence and eugonic characters. We may further suppose that, owing to the great resistance offered by the bovine tissues, the "human" bacilli, in passing through the bovine body, underwent very little multiplication, whereas the "bovine" bacilli flourished and multiplied at a relatively much greater rate, so that ultimately the latter wholly outnumbered the former, and the emulsions or cultures taken from the tuberculous organs of the animals last used behaved as if they contained bovine bacilli only. In other words, the special conditions determining in these passage experiments the replacement of the human by the bovine bacilli, were the presence of both human and bovine bacilli in the original material, and the influence of the bovine tissues, favouring the growth of the latter so much more than that of the former, so as to lead to the complete or almost complete elimination of the human element.

We may thus, (though so far we have met with no direct evidence of the simultaneous presence of bacilli of Group I. and II. in the same patient) explain the results obtained in the above cases by the supposition that in them we have to deal with a mixture of viruses, of a virus from a human source and a virus from a bovine source, each possessing stable characters.

61. On the other hand, if we assume that the characters of the bacillus of tuberculosis (whether human or bovine) are not always absolutely stable (we have seen that some facts point to this) we may adopt the following alternative view:—

We may suppose that, in the case of each of the passage experiments the original material contained only slightly virulent human bacilli, but that these were in a special condition of instability; so that when subjected to certain influences they became modified in character, and transformed into highly virulent dysgonic bovine bacilli, these influences being supplied by the tissues of the bovine animals, through the bodies of which the bacilli were passed.

Similarly we may suppose that highly virulent bacilli from a bovine source, lodged in the human body, may, under certain conditions, manifest instability; may, under the influence of human tissues become modified in character, and so may be transformed into bacilli possessing all the features of the bacilli of Group II.

62. Whether the one or the other of these views is the true one must be decided by the observation of facts. By more than one method, into the details of which we need not enter here, the two views may be tested. By these methods we have made and are making observations, by the help of which we look forward to being able to prove conclusively which of the two views is the true one. But the subject is so complicated, the inquiry so beset with pitfalls in the shape of possible errors, and the conclusion arrived at, whichever it be, so far-reaching in its bearings, that we think it would be unwise, at the present stage of our inquiry, to make any statement whatever about the results which we have so far obtained. At the same time we are unwilling to delay the issue of the present Report until this particular line of inquiry is finished. So as soon as we have completed our observations and are able to deliver a decided judgment we shall report it without delay.

63. It may, however, be worth while to point out the important practical bearings of the inquiry according as the one view or the other is proved to be the true one.

Should it be proved that the cases in question were due to an admixture with the bacilli of human source of a few bacilli of bovine source, the two kinds always remaining distinct the one from the other and never becoming changed the one into the other, we should have no need to enlarge appreciably our conception of the extent to which the human body is subject to bovine tuberculosis. Such cases of admixture must be few and their effect slight; bovine tuberculosis in the human body would practically be limited to cases such as those which furnish Group I.

Should, however, it be conclusively proved that a eugonic bacillus of low virulence may be modified under certain conditions into a dysgonic bacillus of high virulence and *vice versa*, our views as to the relation of human to bovine tuberculosis must be very different. Such a conclusion would lead to the following view. Bacilli from a bovine source entering a human body in scanty numbers may become lodged there without immediately provoking a generalised progressive tuberculosis. During their sojourn there they may become modified into eugonic bacilli of low virulence; and they may then give rise either to a limited tuberculosis only or, under the influence of certain conditions, to a generalised progressive tuberculosis. For some time after the change they may remain unstable and capable of reverting to their bovine character under changed conditions, when subjected for instance to the influence of bovine tissues as in the passage experiments. Or after a long stay in the human body their character may become so fixed that they cannot be distinguished from bacilli conveyed directly from man to man.

It is on account of the far-reaching bearings of the conclusion that we are unwilling to make any statement at all premature.

We may take this opportunity of pointing out that time is an essential factor in dealing with a disease of so chronic a nature as tuberculosis. Some of its problems, such for instance as the possible change in virulence and other characters of the virus obtained from one kind of animal by repeated passage from animal to animal of another species, can only be settled after constant observations extending over a long period of time.

64. Besides the methods described so far by which we have attempted to answer the question whether human and bovine tuberculosis are one and the same, yet other methods are open to us.

It is well known that in the case of many diseases caused, like tuberculosis, by a micro-organism, immunity against the disease may be secured by introducing into the body the micro-organism causing the disease, in such a way and in such a small dose that the disease thereby set up is slight and transient. The results obtained in this way have been so striking as to lead to a general acceptance of the view that a micro-organism which can thus be used to produce immunity against a particular disease may be regarded as identical with the micro-organism causing that disease. Hence if the bacillus of human tuberculosis can be used to confer immunity against bovine tuberculosis, or *vice versa,* we are supplied with a further proof of the identity of the two diseases.

Positive results in this direction have already been obtained by various observers. We are ourselves making careful and extended investigations on the matter; but we are not yet in a position to state the results which we have obtained.

A somewhat similar argument may be drawn from the results of the use of "tuberculin," a preparation obtained from cultures of the bacillus of tuberculosis, the subcutaneous injection of which, in a proper manner, gives rise to a definite reaction in an animal body suffering from tuberculosis, but to no such reaction in an animal body free from tuberculosis. Now the reaction set up in bovine and other animals by tuberculin prepared from human tuberculosis is in every way identical with the reaction set up by tuberculin prepared from bovine tuberculosis.

65. In all which has been recorded above we have limited our inquiry to the identity of human and bovine tuberculosis. But the results at which we have arrived point very strongly to the necessity of extending our studies to the tuberculosis occurring naturally in animals other than man and the ox; and indeed the terms of our reference direct us to do this.

We have already made observations with this intent, and have especially directed our attention to the tuberculosis so common in pigs, a matter of great practical importance. We propose to report on a future occasion concerning this and other matters entailed by the terms of our reference.

Conclusion.

66. We may briefly sum up the bearings of the results at which we have already arrived as follows:—

There can be no doubt but that in a certain number of cases the tuberculosis occurring in the human subject, especially in children, is the direct result of the introduction into the human body of the bacillus of bovine tuberculosis; and there also can be no doubt that in the majority at least of these cases the bacillus is introduced through cows' milk. Cows' milk containing bovine tubercle bacilli is clearly a cause of tuberculosis and of fatal tuberculosis in man.

Of the sixty cases of human tuberculosis investigated by us, fourteen of the viruses belonged to Group I. that is to say contained the bovine bacillus. If, instead of taking all these sixty cases, we confine ourselves to cases of tuberculosis in which the bacilli were apparently introduced into the body by way of the alimentary canal, the proportion of Group I. becomes very much larger. Of the total sixty cases investigated by us, twenty-eight possessed clinical histories indicating that in them the bacillus was introduced through the alimentary canal. Of these thirteen belong to Group I. Of the nine cases in which cervical glands were studied by us three, and of the nineteen cases in which the lesions of abdominal tuberculosis were studied by us, ten belong to Group I.

These facts indicate that a very large proportion of tuberculosis contracted by ingestion is due to tubercle bacilli of bovine source.

A very considerable amount of disease and loss of life, especially among the young, must be attributed to the consumption of cows' milk containing tubercle bacilli. The presence of tubercle bacilli in cows' milk can be detected, though with some difficulty, if the proper means be adopted, and such milk ought never to be used as food. There is far less difficulty in recognising clinically that a cow is distinctly suffering from tuberculosis, in which case she may be yielding tuberculous milk. The milk coming from such a cow ought not to form part of human food, and indeed ought not to be used as food at all.

Our results clearly point to the necessity of measures more stringent than those at present enforced being taken to prevent the sale or the consumption of such milk.

We desire to express in the strongest terms how fully we realise the great assistance which we have throughout received by the unwearied diligence, the tactful and resourceful energy of our secretary, Dr. Steegmann.

We cannot speak too highly of the zeal and ability with which our investigators, Drs. Cobbett, Stanley Griffith, Eastwood, Frederick Griffith and Hammond-Smith, have carried out the tasks allotted severally to them. We have in the course of the inquiry been greatly helped by the suggestions which they have from time to time made, and we feel that their constant and alert co-operation has had a large share in securing whatever value attaches to the result of our investigation. We should like to express also our appreciation of the value of the services rendered by the more subordinate members of the staffs at both farms, more especially by Mr. C. F. Fox and the laboratory assistants at Blythwood, Walpole and Royalcot.

And we cannot refrain from calling attention once more to the unstinted generosity of Sir James Blyth who has ungrudingly extended his hospitality beyond the time first suggested and has with the greatest liberality, met our every wish.

(Signed) M. FOSTER, *Chairman.*

G. SIMS WOODHEAD.

SIDNEY MARTIN.

J. McFADYEAN.

RUBERT BOYCE.

EDWARD J. STEEGMANN, *Secretary.*

January, 1907.

INTRODUCTION.

The Commission was appointed on August 3rd, 1901 and met for the first time on October 18th following.

The first two meetings were occupied with considerations of the means that were to be adopted to solve the problems set out in the reference.

Having been led to understand that the inquiry was expected to be essentially an experimental one, the Commission decided, in the first instance at all events, not to examine witnesses but to institute the fullest possible experimental research in laboratories under its own direct control. It was decided to carry out two independent investigations, one with tuberculosis occurring in bovine animals, and the other with tuberculosis of human origin, the two investigations being kept strictly separate, being conducted at places situated as far as conveniently possible from each other, and each being under the care of a qualified resident investigator.

Immediately after the announcement of the appointment of the Commission had been officially made, various offers were received, on the one hand of places at which experimental work could be conducted, and on the other hand of assistance and co-operation in carrying out experiments in laboratories already established. The latter it was decided not to accept. Each of the former was carefully considered, the Secretary visiting some of them and reporting as to the extent and amount of the accommodation available, and it was eventually decided that the invitation given by Sir James Blyth to occupy one of his farms at Stansted, in Essex, afforded the greatest advantages from every point of view.

The Commission therefore inspected the farm offered by Sir James Blyth, and also a second one in the same neighbourhood which, on learning that two places were required he most generously placed at the disposal of the Commission in addition to the first, and finding that these farms were eminently suitable for the purpose the Commission accepted them and decided to carry out the work there.

THE EXPERIMENTAL FARMS.

Blythwood. The first of these places is known as Blythwood Farm. It is situated close to Stansted in Essex, but the whole of the portion of it in the occupation of the Commission is in the county of Hertfordshire. The total area amounts to about 150 acres, all of which Sir James Blyth was willing to lend, but as there was no necessity for so great an amount of land only a portion of it, amounting to about 19 acres was taken over, including the farm buildings already there. These farm buildings and the land surrounding them had for a number of years been used entirely as a stud-farm for the breeding of horses. They had not been used for keeping cattle for several years, and such buildings as had been at any time occupied by these animals had been practically rebuilt since then.

Walpole. The second farm is known as Walpole and is situated on the further side of Stansted, in the county of Essex, at a distance of about one and a half miles from Blythwood. The extent of the land belonging to this farm is about 14 acres, of all of which the Commission took possession. All the buildings on the farm had been recently newly erected and had never been occupied by cattle.

Royalcot. In addition to these two farms Sir James Blyth placed at the disposal of the Commission a house for the accommodation of the members or any of the assistants, and partially rebuilt and entirely refitted it at his own expense. This house, known as Royalcot, is situated in the village of Stansted, midway between the two farms, and it is here that a third laboratory was subsequently established in which Dr. Eastwood's work is carried out.

All these three places were handed over by Sir James Blyth for a definite period of three years without any payment of rent whatever, and at the end of that time, finding that it was necessary to continue the work, he allowed the tenancy to be continued on similar terms for so long a period as might be necessary. The first Report acknowledged the great help that Sir James Blyth had rendered in giving up these places, and further experience has only served to show that they are most suitable for the purpose, and that his liberality and unselfishness have materially assisted the investigation.

Laboratories, etc.

It was decided to utilise Blythwood Farm for the investigation of tuberculosis of human origin, and to erect laboratories and such additional buildings as might be necessary for carrying out the work. The Commission considered it of great importance to use every care to prevent the spread of infection and decided that all the infected animals should be kept always within the sheds provided for them and on no account be allowed in the fields. It was also arranged that all the litter and refuse from the stalls and sheds in which the infected animals were kept, as well as the carcases of such animals after being killed and all infected matter, should be destroyed by fire. For this purpose a specially designed destructor was erected to consume the material to be destroyed without creating any nuisance in the neighbourhood.

The portion of the farm occupied by the Commission is divided by a road passing from London to Cambridge. The part of it containing all the original buildings is situated on one side of this road, and this portion of the farm it was decided to use as the experimental side, reserving the other, on which several cow-sheds were erected, as a quarantine station in which to keep stock animals before inoculation. Throughout the whole of the work no animals which had once been taken to the experimental portion of the farm have ever been removed from it, all the carcases of animals that have died or been killed having been burned in the destructor.

The laboratory originally erected has been from time to time enlarged as occasion arose, and it has proved necessary during the prolonged period of the experiments to erect additional sheds or cages to accommodate the increased number of animals used.

A special building was erected in which to carry out the post-mortem examinations of the larger animals, and this was put up in close proximity to the destructor so that such portions of the animals as it was not necessary to preserve could be destroyed at once without being carried to a distant part of the farm.

Owing to the difficulty of obtaining a supply of gas for lighting and laboratory purposes it was necessary to instal an apparatus for making gasolene. This proved fairly satisfactory for some time, till a proper supply of ordinary coal gas, which experience has proved to be far more convenient and satisfactory, was obtained.

A laboratory, post-mortem house and destructor of exactly similar design to those at Blythwood were also erected at Walpole, and various alterations were made to the existing buildings to fit them for the purposes of the inquiry.

At a subsequent period it was found that Walpole was not quite large enough to accommodate all the experimental animals needed as well as the stock animals which it was necessary to keep there. Sir James Blyth again came to the assistance of the Commission, and granted an additional large field on which cow-sheds were erected.

Cow Sheds.

Since it had been already decided to keep all the infected cattle under cover, and not to allow them to be in any of the fields, special care was taken in designing the sheds in which they would have to be kept. The existing stalls which had been designed for horses were easily adapted by erecting divisions to make separate places, each to contain one or two animals, and by covering the floors with hard and impervious material. Each of these places has a separate entrance and the drainage from each passes direct from it. The new cow-sheds that were erected both at Blythwood and Walpole were designed to give the greatest amount of light and ventilation, and to keep the animals as far as possible separate from each other.

Although every possible despatch was used some considerable time was necessarily occupied in erecting the various buildings and making the alterations that were required, and it was not till April 1902 that the actual experimental work could be commenced at Stansted. The present Report is therefore based on the work that has been done between that time and November 1906, a period of about four and a half years. The details of this work are set out in full in the various volumes of the Appendix, but it is desirable to give a short description of the administration of the farms and laboratories and the methods adopted in carrying out the inquiry.

RESIDENT STAFF.

As already stated it was decided that the whole of the experimental work should be done, under the direct supervision and control of the Commission, by qualified investigators residing at Stansted, and it was further considered that it would be an advantage if the work of erecting the buildings and laboratories should be supervised by those who would have to occupy them. As soon as possible, therefore, after the first meeting, Dr. E. St. B. Sladen and Dr. Louis Cobbett were appointed to take charge respectively at Blythwood and Walpole Farms. Owing to ill-health Dr. Sladen was obliged to resign his appointment when the experimental work at Blythwood had only been in progress for a few months, and on his retirement Dr. Cobbett took over the charge of Blythwood. Dr. A. Stanley Griffith was then appointed to carry out the investigations at Walpole.

It subsequently become necessary, owing to the increase of the work, to obtain additional qualified assistance, and Dr. H. J. Hutchens was temporarily appointed to carry out certain special work at Blythwood under Dr. Cobbett's supervision, and Dr. F. Griffith was permanently appointed as assistant to Dr. A. S. Griffith at Walpole.

After the commencement of the systematic work at Blythwood and Walpole the Commission realised the necessity of having a third laboratory, totally distinct from either of the other two, in which purely comparative work should be carried out on material supplied from them. It was decided that this comparative work should at the commencement deal with the histology of the lesions produced by the two chief types of tuberculosis dealt with, namely, that obtained from human and that obtained from bovine sources. To carry out this investigation additional laboratory accommodation was erected at Royalcot and placed under the charge of Dr. Arthur Eastwood. Dr. Eastwood's work was subsequently extended to a comparative study of the cultural characters of the different viruses, both human and bovine, and the results of all his investigations are published in Volume IV. of the Appendix.

At the end of September 1906 the Commission, to their great regret, lost the services of Dr. Cobbett on his appointment to the Chair of Pathology at the University of Sheffield, and Dr. Stanley Griffith succeeded him in the charge of the work at Blythwood, whilst Dr. F. Griffith took over entire charge at Walpole.

Almost the whole of the work carried out at Blythwood, referred to in the Report and detailed in the Appendix, has been done by Dr. Cobbett. The experiments on the modification of virulence in the living animal which are not dealt with fully in this Report have also been conducted by him. Although he is unable any longer to take an active part in the work at Stansted, Dr. Cobbett will be informed as to the progress of the continued research on this question, and the Report he has submitted to them on the experiments already done will be included in the Appendix to a subsequent Report in which this question will be considered by the Commission.

The whole of the investigations at Blythwood, Walpole and Royalcot have been carried out under the direct control of the Commission and all experiments have been arranged by them. But while maintaining a close supervision over the whole of the work, the Commission has felt it desirable to allow the investigators considerable latitude in carrying out the details of the various experiments, and has repeatedly profited by the suggestions made by them. The fact that none of the investigators, though experienced in bacteriological methods and accustomed to original research, had been specially engaged in investigations regarding tuberculosis, and that they all commenced the work with unbiassed and open minds, has been of advantage. In an investigation extending over so long a period and covering so large an extent of scientific ground it is natural that the views of the investigators should not in all cases be wholly in accordance on certain minor points, but the Commission has considered it right to allow each one of them to set forth not only the definite facts arising out of the experimental work but also his own views based on the work done by himself.

The great number of animals both stock and experimental which had to be kept at the two farms, and the number of unskilled labourers employed, made it necessary to obtain the help of an experienced farm manager, and Mr. Keddie, who was already well acquainted with both farms, was appointed to take charge of such matters as were outside the experimental work. Mr. Keddie's exceptional knowledge of cattle and their proper management has been of material help.

Skilled assistants were engaged to work in the various laboratories, Mr. C. Attoe at Blythwood, Mr. Peckham and Mr. Clark at Walpole, and Mr. Nicholls at Royalcot. They have all carried out the work entrusted to them in this capacity entirely to the satisfaction of the Commission. A varying number of junior laboratory assistants have also been employed from time to time as necessity arose. Mr. C. F. Fox was appointed to assist in keeping the records and taking notes, and the ability which he has displayed in carrying out his work has been very marked.

One of the greatest cares has been to prevent even the suspicion of infection from one farm or laboratory being conveyed by any means to another, and to attain this the most careful precautions have been carried out throughout the whole of the investigation. The staffs both of scientific assistants and farm labourers at each of the separate places at Stansted have been kept entirely distinct and apart from each other, and no man working at one has been allowed to visit another. In addition the men actually engaged in contact with the infected animals have been supplied with complete suits of washing material which they put on when commencing their work and take off when leaving the farms. The members of the Commission on their frequent visits to Stansted have, so far as possible, avoided going to one farm on days when they were conducting post-mortem examinations or examining infected animals at another.

EXPERIMENTAL ANIMALS.

Although the work has been mainly concerned with the tuberculosis of bovines the Reference instructed the Commission to enquire into tuberculosis in animals generally, and it was therefore necessary to carry out experiments on various species.

Bovines. With regard to bovines the Commission carefully considered the particular kinds which should be used for the experiments. The important point was to be able to obtain a sufficient supply of such animals so far as possible free from tuberculosis before they came to the farms, and the great difficulty which would be experienced in doing this if they were obtained from the ordinary sources was fully realised. Almost all the cattle used from the commencement of the inquiry up to the present time have been Jerseys, which are remarkably free from tuberculosis. All these animals were imported direct from Jersey with the most careful precautions to prevent the possibility of infection on the journey. Mr. Keddie has in all cases himself gone to the island and selected such animals as were required. They have been brought over from time to time in lots of from twenty to twenty-five and from the hour of leaving the island to their arrival at Stansted they have been under Mr. Keddie's immediate care, and in the case of calves have been fed on the journey with milk conveyed in special cans belonging to the Commission.

The occurrence of tuberculosis among Jersey cattle in the island is extremely rare, but in order to reduce to the minimum the risk of experimenting on animals already infected, further precautions on receiving the animals at the farms have been adopted. Every bovine animal used has been tested with tuberculin on the quarantine side of the farm before being taken to the other side. The test has always been postponed till the animal had entirely recovered from the fatigue or other effects of the journey, and become accustomed to its new surroundings, and also till repeated observations had enabled the normal temperature of each individual animal to be determined. As a rule the tuberculin test has been carried out about three weeks after arrival at Stansted.

The procedure adopted both at Blythwood and Walpole for carrying out the tuberculin test on the non-infected animals is as follows:—

Tuberculin Test.

The temperatures are taken at 10 a.m. for a varying period of from one to two weeks before the test, and no animal is tested unless its temperature is normal and regular, and it appears to be in every way in good health. On the day of the actual injection of tuberculin the temperature is taken twice, once in the morning and the second time at 5 o'clock in the afternoon. Immediately after taking the temperature for the second time the tuberculin is injected. The first record of the temperature after injection is taken six hours later, that is about 11 p.m., and after this the temperature is noted every three hours until 5 o'clock the following day. By this means a record of the temperature is obtained for a period of twenty-four hours after the injection of tuberculin.

The procedure for the infected animals is the same but as in these cases the temperature before the injection of the tuberculin is frequently abnormal the test is not delayed on this account, as in the case of the non-infected animals.

All the tuberculin used has either been obtained from the Royal Veterinary College, or prepared by the Investigators in the laboratories at Stansted.

A considerable amount of information has in this way been obtained as to the value of the tuberculin test as a means for detecting the existence of tuberculosis in bovine and other animals. This matter will be dealt with in detail in a future report. For the present it will be sufficient to express the opinion that the test is one of great value when properly carried out.

It will be noted on reading the detailed post-mortems of the various bovine animals included in the experiments that in most cases they were tested with tuberculin before being killed, and in some instances were tested more than once during the period of infection. In the earlier part of the investigation all the infected animals were tested before being killed in order to gain information as to the result of the test, as well as for a diagnostic purpose, but this was not done in all subsequent cases. Many animals in which the disease was acute and which were in an apparently dying condition before being killed were not tested after inoculation, but without exception all the bovines, and most of the larger animals such as pigs, dogs and goats, were tested before being used for experimental purposes.

Objection might be taken to the almost exclusive use of Jersey cattle for experiments with tuberculosis on the ground that these animals are supposed to be especially susceptible to the disease. But in the course of the inquiry a number of experiments on Shorthorn cattle have been carried out, sufficient to prove that this fear is unfounded, and that there is no reason to think that Jersey cattle are naturally more susceptible to tuberculosis than other breeds.

In addition to bovines, monkeys, pigs, goats, dogs, cats and various other animals have been used for experimental purposes.

Anthropoids.

Experimental investigations have been carried out on a considerable number of Anthropoids, all of which, with the exception of two, have been chimpanzees. The two exceptions were ourang-outangs, and the experience with these two did not encourage a further use of this species, since they are difficult to keep in captivity. Both the specimens died before any experimental results had been obtained from them.

The chimpanzee appears to be the most suitable of the anthropoids for experimental research. It is the most easily obtained of all of them, and with proper care is not difficult to keep in captivity. In addition, experience has shown during the inquiry that it is rare to find a chimpanzee affected with tuberculosis unless it has been for a considerable time in captivity and in contact with men; and the experience of others confirms this. One observer has stated that in over 100 specimens examined by him (which had been used for experiments not connected with tuberculosis), in only two did he find post-mortem evidence of the disease.

Monkeys.

The early experiments on these animals were done with the ordinary species used in laboratory work, namely, the common Indian Rhesus (*Macacus Rhesus*), an animal which is imported in large numbers and which can nearly always be easily obtained. It seemed desirable however to extend the investigations to other kinds of monkeys, and in order to do this it was necessary to select a species a sufficient number of which could be obtained without difficulty, since it was obviously useless to experiment on isolated specimens of different kinds. The common African dog-faced baboon (*Papio Porcarius*) which may be obtained with no great difficulty, and the lemur, of which sufficient numbers could be got from time to time, were therefore selected.

With regard to the Rhesus a serious difficulty was met with at an early stage of the investigations. Several lots of these monkeys having been purchased from the ordinary dealers, and one or two of each lot having been used for experimental purposes, it was found that some of the others with which they had been in contact subsequently developed spontaneous tuberculosis, thus throwing doubt on the results caused by the inoculated disease in the experimental animals. This matter is referred to in the experiments on monkeys at Walpole with the virus known as B.1.

It was found that the tuberculin test in monkeys cannot be relied on in all cases, however carefully carried out. In some instances marked reactions were obtained after the tuberculin had been injected into monkeys in which no tuberculous disease was found on subsequent post-mortem examinations, and on the contrary, a reaction occasionally failed to appear in animals which were subsequently found to be extensively affected. It was also found from repeated observations that the natural temperature of a Rhesus monkey varies very considerably at different times in the day. It was eventually decided that, it being necessary to continue the observations on monkeys, the best means to adopt for obtaining healthy animals would be to keep them under observation for prolonged periods before using them for experimental purposes, and to use only such animals as gave every evidence of being in good health, such as growth, increase of size and weight, and good appetite.

A quarantine station was therefore established in a suitable place at Isleworth, and cages were erected there in which monkeys could be kept under the healthiest possible conditions. All these animals used during the greater part of the investigation had, previous to each experiment, been under observation for periods of in all cases more than three months and in many for a much longer time at this quarantine station. Before being used for experimental purposes they were also tested with tuberculin, and as an additional precaution one or two animals out of each lot purchased together were killed from time to time and examined. If any one of these animals was found to show any evidence of natural tuberculosis none of its fellows was used for experimental purposes.

The ordinary Rhesus monkey used for laboratory work is as a rule a young animal. The Rhesus grows to a large size, and when adult is savage and difficult to handle. On two separate occasions a number of adult Rhesus monkeys, specially obtained, were imported direct from India. These animals were caught in places as far as possible remote from human habitations and were brought to this country in separate cages, every precaution being taken to avoid the risk of infection on the journey. They arrived at the quarantine station in all cases within two months of the time of being actually caught, and yet on both these occasions one or two of the animals on arrival appeared to be in bad health, and on being killed were found to be suffering from extensive tuberculosis. Their fellows were all killed at the quarantine station and nearly all of them were found to be similarly affected. An interesting point about this experience was that in nearly all the cases some of the tuberculous lesions found on post-mortem examination were calcareous, and it seemed not unlikely that the diseases in these animals had been contracted at a period prior to the time when they had been captured. The experience gained during the inquiry shows that the young freshly imported Rhesus monkey is more likely to be free from tuberculosis than the adult animal of the same species; but the conditions under which these young animals are brought over, large numbers being packed together in small cases and the cases themselves being stowed frequently in unsuitable parts of the ship in which they are conveyed, tends to make it somewhat difficult to obtain really healthy specimens. Some of the experiments in feeding young Rhesus monkeys with tuberculous milk were carried out on animals which had actually been born in the quarantine station, whose mothers, when killed, were found to be entirely free from tuberculosis.

Various monkeys which died, or were on account of apparent ill-health killed, in the quarantine station were found to be suffering from diseases other than tuberculosis, and some doubt was caused at one time by the occurrence of a peculiar condition in the lungs of Rhesus monkeys which bore some slight resemblance to tuberculosis. Small tubercles were found in the lungs which on microscopic examination were found to contain an acid-fast organism closely resembling in appearance the tubercle bacillus. Inoculations of emulsions containing this bacillus failed however, to produce tuberculosis in guinea-pigs. Careful examination by Dr. Griffith of these tubercles revealed the presence in each of them of a small cyst containing a living parasite hitherto unidentified. As this discovery had no special bearing on the work of the Commission a description of it was allowed to be published in Memoir No. 18 of the Liverpool School of Tropical Medicine.

The pigs used were obtained locally in the neighbourhood of Stansted, and had all been bred for the purpose of being eventually killed and used for food as pork or bacon. Some of the animals were of the breeds known as Berkshire or large White Yorkshire. Others were of the breed peculiar to the district known as black and white Essex, and a few were cross-bred Yorkshire and Berkshire, or Yorkshire and Essex. The young animals when purchased were from six to eight weeks old, and in all cases entire litters were obtained, some of them being used for experimental purposes and one or two of the same litter being retained as controls. No pigs have been bought from farmers or others who have kept at the same time dairy cows, so that in all probability none of the pigs used had ever received any cow's milk as food before arriving at the farms of the Commission. Particular importance was also attached to purchasing only such pigs as had not been castrated, to avoid any possible infection through that operation. Pigs.

A considerable number of experiments have been made on goats of different ages, all the adult animals having been obtained in the neighbourhood and some of the young ones having been bred at the farms. Goats.

Dogs.

The dogs which have been used were obtained elsewhere than at Stansted. Most of them had been kept for some time in the Quarantine Station at Isleworth before being sent to the farms, and almost all the puppies used had either been born or kept there for the first few weeks of life. The mothers of all the puppies have been under observation.

Guinea-pigs and Rabbits.

During the greater part of the time over which the investigation has extended a large proportion of the rabbits and guinea-pigs used in the experiment have been bred at the farms.

METHODS OF EXPERIMENT.

In considering the methods of inoculating animals which should be adopted it was decided to use five different ways of producing artificial infection, namely, feeding and subcutaneous, intramammary, intravenous and intraperitoneal inoculation. No use has as yet been made of inhalation as a means of infection, the great objections to this method being the difficulty of estimating the dose and the danger of the spread of infection to other animals.

Feeding.

The feeding experiments have been of considerable extent, especially at Walpole, and are detailed in the Appendix. They have included feeding for prolonged periods, in some cases extending to months, as well as feeding by single doses of large or small amount. They have been carried out on animals of different species as well as of different ages. At Walpole the tuberculous virus has been given by the mouth in the form of milk from infected cows or measured quantities of culture, but at Blythwood, in addition to this, the tuberculous virus contained in human sputum has been given mixed with food.

Inoculations.

It is not necessary to describe in detail the methods of inoculation used or of the stringent precautions always adopted in carrying them out.

In the case of intramammary injections where the cow has, at the time of inoculation been suckling a calf, the calf has been removed from its mother immediately before the injection and not allowed again to suck from her till after a period of twenty-four hours, when there could no longer be any risk of it obtaining any of the artificial virus injected.

Estimation of Dose.

The earliest inoculation experiments consisted in injecting measured quantities of emulsions made either from the original material received at the farms or from material derived from lesions produced in animals such as guinea-pigs by infecting them with the original material. The emulsion before injection was always examined microscopically, and the amount given depended upon whether it contained tubercle bacilli in large or small quantities. Considerable difficulty was found at first in estimating the actual numbers of bacilli contained in such doses. Subsequently, however, after many experiments by Dr. Eastwood, a method devised by him for counting the numbers of bacilli contained in any given emulsion was adopted. This method is described in Dr. Eastwood's Report on the Enumeration of Tubercle Bacilli given at the commencement of Vol. I. of the Appendix. The following brief description of the method of preparing the emulsions from fresh material applies to both Blythwood and Walpole.

The material on arrival is carefully examined, and the portions are selected which are to be used for sowing cultures and making emulsions. The surfaces of these parts, after the removal in the case of glands of all surrounding fat, are seared with a Paquelin cautery and pieces of the tuberculous tissue are removed through an incision made in the centre of the seared area. The pieces to be used for sowing cultures are placed in a small test tube, and those from which the emulsion is to be made are put in a sterilised porcelain mortar. In the mortar the tissue is first reduced to a pulp with a glass pestle, and then emulsified with sterile salt solution. The emulsion so made is then filtered through sterilised muslin into a sterile cylindrical measure to strain off the coarser particles, and is put on one side for a sufficient time to allow the finer particles of tissue to settle.

When this precipitation has taken place the supernatant fluid is poured off into a sterilised flask or beaker and is ready for injection. Before being used for inoculating animals, the emulsion is thoroughly shaken for some time in order that the tubercle bacilli contained in it may be distributed throughout the fluid as evenly as possible.

In the earlier experiments, after a microscopical examination of the emulsion so prepared had been made, it was at once used for injection into animals; but subsequently, the emulsion having been made in the morning, a small quantity was examined by Dr. Eastwood by the method already referred to, and the actual injection into animals was not made until his report on the number of bacilli contained in a given quantity was received at the farms. The actual dose then given to the animals was based on the enumeration so made.

The methods used for preparing cultures from the original material are described in the Reports on cultures given in Vol. III. of the Appendix. It was found impossible in spite of repeated attempts to obtain a reliable method for enumerating the actual number of tubercle bacilli contained in any given measure of culture. When cultures are used for inoculation or feeding the doses in all cases are expressed in milligrammes. The method for obtaining accurate doses is described by Dr. Griffith under the head of Methods of Inoculation at the commencement of Vol. I of the Appendix. A similar method was used at Blythwood and the description of it at one place applies equally to the other. It will be seen from this account that in reality, although the doses are expressed in milligrammes, cubic millimetres would be more correct, but the results obtained by the volumetric method are in the closest possible agreement with those that would be obtained by the gravimetric method, as was proved in one instance in which the culture was first actually weighed and then estimated by the method described by Dr. Griffith.

It is not possible to give an actual comparison between the doses given in emulsion with those given in culture. It may, however, be stated definitely that the great majority of culture inoculations have contained far larger numbers of tubercle bacilli than the largest doses of tissue emulsion.

Material used for Experimental Purposes.

The material of which use has been made in the experiments has been obtained almost entirely in London.

The specimens of bovine tuberculosis used have come with one exception from the Royal Veterinary College or from the Metropolitan Meat Market. A very large number of specimens has been examined, and altogether thirty different viruses of bovine animals have been used for experimental purposes. The details of these different viruses are given in the Table of Origins, in Volume II. of the Appendix. Bovine.

The specimens obtained from the Veterinary College were all from animals known to be diseased before death, but those which were obtained from the Metropolitan Meat Market came from the bodies of animals which had been sent there for the purpose of being killed for food, but in which tuberculous disease was found to exist by Mr. King, the Chief Veterinary Inspector, or his assistants when making their usual examination of the carcases before allowing them to leave the slaughter houses. All the carcases from which specimens were obtained had already been condemned as unfit for human food before any portions of them were selected for investigation. The assistance received from Mr. King and the authorities of the Metropolitan Meat Market, the trouble which they have taken in reserving material for inspection, and the facilities which they have put at the disposal of the investigators have been of very material benefit to the work of the Commission.

The human viruses have been obtained from various sources, chiefly from the London hospitals and infirmaries, and the Commission desire to record their Human.

appreciation of, and gratitude for, the great help received from the authorities of these institutions by their cordial co-operation in the inquiry.

The Secretary has been notified regularly of operations or post-mortem examinations on cases that might possibly provide material such as it was desired to obtain, and the clinical investigator, Dr. Hammond-Smith, has always been allowed to attend these operations or examinations, and every opportunity has been given to him for inspecting records and clinical notes.

The number of different viruses actually used, amounting in all to sixty, is only a portion of the total number which has been received and investigated. The cases have not been specially selected, but those which were not used for actual experimental work were rejected after careful examination for various reasons, such as the small amount of disease present, or the possibility of decomposition having already commenced. The order in which the different viruses appear in the third volume of the Appendix is the order in which they were received from time to time at Blythwood. They are representative of the chief types of tuberculosis as commonly found in the human subject in this country, and they have been obtained both from the operating theatre and the post-mortem rooms as well as, in the case of sputum, from hospital wards.

Some of the patients from whom material used for experimental purposes was obtained by operation, have been kept under observation for considerable periods and visited at intervals by Dr. Hammond-Smith. In one case in which cervical glands removed from one side of the neck were used at Blythwood, glands were obtained from the other side after a second operation a year later.

The details of the various viruses of human tuberculosis are given in the Blythwood Table of Origins at the commencement of Volume II. of the Appendix.

Carriage of Specimens.

The material from which viruses experimented with have been obtained has, in the case of material derived from operations, almost always been received at the laboratories on the same day as that on which it was removed from the patient, frequently within a few hours. In the case, however, of material obtained from post-mortem examinations greater delay has occurred owing to the rule obtaining in most hospitals that post-mortem examinations are not performed till after the lapse of some considerable time after death. In cases where information has been received of the death of a patient precautions have been taken to prevent as far as possible decomposition of the body taking place before the post-mortem examination. In hospitals unprovided with refrigerating chambers the bodies have been surrounded by blocks of ice and practically frozen by this means.

Special carrying boxes were designed by the Commission for conveying the material collected to the farms. The boxes contain a metal vessel with an air-tight cover in which bottles containing the material, or, in the case of large specimens such as lungs, the material itself, is placed mixed with ice. The space between the metal vessel and the sides of the box is filled with non-conducting material to prevent the melting of the ice. The metal vessels are always carefully sterilised and hermetically closed at the laboratories at Stansted before being returned to London for further use, and for each separate case newly sterilised bottles which have not been previously used are employed. The boxes are locked after the material is placed in them in London, and opened by duplicate keys at the laboratories, and entirely distinct sets of boxes are used for the two farms.

By the courtesy of the authorities of the Great Eastern Railway Company the usual formalities necessary to the ordinary railway parcel service have been dispensed with, and the locked boxes containing the specimens have been sent from London to Stansted with the minimum amount of delay.

STATISTICAL INQUIRY.

In studying the statistics of the occurrence of different types of tuberculosis as shown by the registers of death, the Commission considered that it would be of use to obtain more detailed information if possible, as to the real extent of abdominal tuberculosis as shown by post-mortem examinations. For this purpose various large towns containing hospitals in which post-mortem examinations had been made for a long period of years were selected, and the services were obtained, in each of these places, of a pathologist to examine the records for a definite past period and, so far as possible, to find out from them the apparent primary seat of the disease in patients who died from tuberculosis, or in whom evidence of this disease was found after death. A large number of records dealing with the subject has been received and will be dealt with in a subsequent Report. But the value of the information thus obtained has not been so great as had been hoped, owing to the fact that in the majority of hospitals the post-mortem records do not appear to have been made in such detail as would enable an opinion to be formed as to the age of the tuberculous lesions.

Special Investigations other than Those at Stansted.

Certain researches which the investigators were unable to undertake in addition to their own particular work have been carried out for the Commission by other observers in their own laboratories.

One of these, an endeavour to obtain uniform emulsions of cultures by a particular method, was done by Dr. Nuttall of Cambridge. The results of this were negative.

Dr. James Miller, of Birmingham, has carried out an investigation including, amongst other matters, the effect of leucocytes in hanging drop preparation on tubercle bacilli of human and bovine origin. The results of this investigation are not yet sufficiently complete to be included in the present Report.

In addition to the pathological and bacteriological problems the Commission desired to investigate certain points connected with the chemistry of the tubercle bacillus. Dr. Griffith carried out at Stansted an investigation concerning the change in reaction produced in broth by the tubercle bacillus, suggested by the work done by Dr. Theobald Smith in America. The results of this work are given in Vol. III. of the Appendix.

The laboratories not being equipped with the apparatus necessary for the more delicate chemical problems, Dr. Harden, D.Sc. of the Lister Institute, at the request of the Commission, carried out a series of preliminary investigations, working on cultures of tubercle bacilli grown in the laboratories at Stansted, with a view to investigating their chemical products. These preliminary investigations having shown that the methods proposed by Dr. Harden would be likely to produce valuable information he is, at the request of the Commission, carrying out a similar research on a more extensive scale at the Lister Institute.

A BRIEF HISTORICAL SKETCH.

From the very earliest times certain cases of wasting of the body, consumption, *phthisis,* were known to be characterised by a diseased condition of, or by morbid growths in the lungs; hence such cases were often spoken of as cases of pulmonary consumption, *phthisis pulmonalis.*

From the very earliest times also, among the morbid growths or changes appearing in various parts of the body, certain kinds were distinguished as of white, creamy, or cheesy-looking, taking the form of lesions which were not abscesses, and whose development, was not accompanied by the heat of inflammation. To such growths or lesions Galen, translating the Hippocratic term χοιράδες*, gave the name *scrofulæ.* And some connection between scrophulæ and pulmonary consumption was admitted or suspected by many observers.

Towards the end of the eighteenth century, the word "tubercle" (tuberculum) which had of old been used by the anatomists to denote any small rounded outgrowth or prominence began to be applied to certain lesions or growths in the lungs. It was so used by Stark (1785), and indeed had been so used a century before by Sylvius (1695); but the first detailed account of "tubercles" in the lungs was by Matthew Baillie in 1794. He describes them as being at first very small, no larger than the head of a very small needle, but subsequently growing much larger and often undergoing transformation into scrofulous abscesses. In this condition they are, he says, the cause of pulmonary consumption, so common in England.

A little later (1803-5) Bayle in France discussed more fully the nature of the minute transparent, grey tubercles, of the size of a millet seed (hence the name miliary tubercles) found in the lungs. He recognised, and this was a most important step, these tubercles as being the outcome of a specific morbid tendency, a tuberculous diathesis. At about the same time the great French physician, Laennec, took up the subject from the clinical as well as from the anatomical side. In the lungs, besides the minute grey tubercles or granulations, the miliary tubercles of Bayle are found other tubercles opaque and yellow, of various sizes, often softening into cheesy caseous material and ultimately giving rise to cavernous abscesses. In addition to the circumscribed tubercles, the substance of the lung may be infiltrated by a caseous scrofulous, or scrofula-like material, Laennec discussed the relations of these various forms of tubercle to each other and to scrofula in general; he studied the relation of these lesions in the lungs to similar lesions in other parts of the body; and he was led to the conception of a genetic primal tuberculous material which, given off by one tuberculous lesion, might be carried to another part of the body and set up tuberculous lesions there. Thus took shape the idea of *tuberculosis* (the word itself was introduced by Schonlein much later), of a specific something which manifests itself by morbid processes, of which "tubercles" form a conspicuous part, and which is infectious in the sense at least that it can spread from one part of the body to another, and in some way can invade the body from without. Thus a scientific explanation was offered of the very widespread belief that pulmonary consumption, the commonest manifestation of tuberculosis, was contagious, and could be conveyed from one person to another.

Some years later (1857) Buhl gave a definite expression to the view foreshadowed by Laennec. He maintained that each of the caseous lesions in the several parts of the body might act as centres in which a tuberculous virus was generated. The virus absorbed into the blood from these centres, and distributed through the blood stream over the body, gave rise in various tissues and organs to new tuberculous lesions, namely, to miliary tubercles, each of which might, by becoming caseous, serve as a fresh centre for the distribution of the tuberculous virus.

(* "Little pigs" ; the reason of this simile is obscure.)

The great development of pathological histology in the middle years of the nineteenth century, due largely to the classic researches of Virchow, while it largely extended our knowledge of the minute anatomy of tuberculous lesions, to a certain extent gave a wrong bent to inquiries, by concentrating the attention of observers too much on the study of anatomical characters and to the conclusions which might be drawn from them, the teachings of clinical and experimental study being for a while somewhat neglected. Thus Virchow himself, laying stress on general pathological processes as the expression of the perverted general activities of the cells of which the tissues are made up, was led to regard miliary tubercles as the only true tuberculous lesions. He held that caseous and scrofulous deposits and infiltrations not originating in miliary tubercles were not in any way specific in nature, but examples of the general decay to which new morbid formations were subject. We find in the history of the various views put forward during this period an example, and many others may be found, how general deductions based on anatomical observations are apt to lead the inquirer astray, in the absence of the more direct knowledge gained by experiments on living animals.

From very early times the experience of the slaughter-house had shown that the lungs of cattle were the seat at times of morbid growths or deposits, of various sizes, forms, and consistency, some being of the nature of abscesses; and as veterinary science gradually developed, "pulmonary phthisis" became a common term in respect to cattle. When in the first half of the nineteenth century these morbid changes in the lungs of cattle began to be studied in the light of the new ideas concerning human tuberculosis, most of the observers came to the conclusion that cattle were subject to a tuberculosis of the lungs identical with the tuberculosis of man.

All observers, however, were not agreed upon this point; and, indeed, a decision was rendered difficult by the frequent occurrence in cattle of a striking affection of the peritoneal cavity, characterised by abundant outgrowths from the serous surfaces, an affection which, known in earlier times as the "French disease," and supposed then to be connected with syphilis, was called in English "Grapes," and in German *Perlsucht,* from the pearl or grape-like appearances of the transparent outgrowths. Some observers maintained that this affection was essentially a form of tuberculosis and that accordingly the tuberculosis of cattle was the same thing as the tuberculosis of man. Other observers, on the contrary, insisted that this abdominal affection had no connection whatever with tuberculosis; and some of these were led further to doubt whether the lung tuberculosis of cattle, which certainly seemed to be akin to the abdominal affection, was really identical with that of man.

Thus, in the earlier years of the latter half of the nineteenth century, while it was admitted that man was subject to tuberculous deposits or growths in various parts of his body, due to the working of an agency, the exact nature of which was obscure, and that cattle were subject to a disease, the manifestations of which were in many respects similar, it was by no means clear that the two diseases were one and the same. Further, while there were some rough indications that the disease could be conveyed from individual to individual, the exact proof of this was lacking.

In 1865 the predominance of the anatomical over the experimental method of studying tuberculosis was suddenly put an end to. In this year Villemin made known that he had succeeded in making rabbits tuberculous by the subcutaneous injection of tuberculous material obtained from cases of phthisis in man, control animals remaining free from tuberculosis. He obtained the same results by the injection of tuberculous material from oxen suffering from grapes. He was able to infect guinea-pigs also by the same method, and, though with much less certainty, dogs and cats.

He observed that tuberculous processes constituting a local lesion were set up at the seat of inoculation, and that later on, after a period of incubation, the tuberculosis spread over the body generally. He recognised these events as showing that a something infectious was introduced with the tuberculous material, that this something reproduced itself at the seat of inoculation, giving rise to the local tuberculosis, and subsequently was carried from the local lesion, probably by the blood stream, to distant parts of the body, setting up tuberculosis at the points where it was arrested. He even went so far as to suggest that this something was of the nature of a living organism.

Villemin's results, on being made known, gave rise at once to great experimental activity and to much controversy. Some observers confirmed Villemin; others maintained that he had been mistaken, since, on the one hand, they failed to set up tuberculosis by the injection of tuberculous material, on the other hand, they found that tuberculosis could be set up by the subcutaneous injection of material which was not tuberculous, such as various non-tuberculous products, pus and the like, or even of wholly inert matters.

Among the many investigations thus set on foot, two call for special mention.

Chauveau in 1868 showed that heifers might be rendered tuberculous not only by subcutaneous or intravenous injection, but also by the simple plan of feeding. He fed heifers with the tuberculous material obtained from cases of abdominal tuberculosis in the ox; these became tuberculous while control animals remained free from tuberculosis. Chauveau also made a more general contribution to the subject by the researches in which he brought forward reasons for thinking that in contagious diseases the "contagium" was of a particulate nature, consisted of solid particles, not of a something dissolved in a fluid.

In 1877 Cohnheim and Salamonsen (repeating, though unaware of doing so, in a more complete manner, an experiment made five years before by Armanni), introduced into the anterior chamber of the eye of a rabbit a minute fragment of tuberculous material obtained in as fresh a condition as possible. The immediate effects of the slight operation, conducted with all necessary precautions, soon passed away. The minute fragment, visible in the anterior chamber, could be seen to diminish; it might even disappear altogether, being wholly absorbed; and for a while no effects at all seemed to have been produced. After the lapse, however, of some days, granulations appeared on the iris, the aqueous humour became cloudy, and upon examination the eye was found to be the seat of a tuberculosis developing in the clearest manner. In different rabbits, the subsequent progress of events differed; but in many cases the local affection of the eye was followed by a fatal generalised progressive tuberculosis of the body. No such tuberculous affection of the eye with consequent results followed the like injection of material not tuberculous in nature, or even of tuberculous material itself, provided that that material had been previously boiled for an adequate time.

This research was of the greatest value since it allowed a test experiment to be carried out with every possible precaution, and the whole process to be actually observed by direct inspection at every step. Cohnheim expounded in a most lucid manner the bearings of the results which he had obtained, showing how they clearly demonstrated the infectious nature of tuberculosis, and how they pointed to the agent of the infection being a micro-organism.

The deduction drawn by Cohnheim was soon proved by actual observation. More than one observer claimed to have discovered in tuberculous lesions a micro-organism possessing the sought for infective properties; but our knowledge of the true organism dates from 1882, when Koch gave the first account of the researches which had led him to detect in all tuberculous material examined by him the presence of a bacillus with special characters, since known as the *bacillus tuberculosis.*

By employing special methods of staining he was able to prove the presence of this bacillus in both the miliary grey granulations and in the caseous deposits of the lungs, in the tuberculous lesions of the liver, spleen, kidney, lymphatic glands, and other organs, and in the sputum of phthisical persons. He found the bacillus present in the tuberculosis, not only of man, but also of monkeys, oxen, pigs, cats, rabbits, guinea-pigs, and of fowls. By making use of solidified and sterilised serum, he was enabled to obtain pure cultures of the bacillus; and these cultures injected into the bodies of guinea-pigs and other animals gave rise to tuberculosis.

With this discovery of the bacillus by Koch our knowledge of tuberculosis became at once sure and precise. It was clear that the disease was due to the action of the bacillus on the organism which it had invaded; we were henceforward furnished with definite criteria enabling us to judge whether lesions were really tuberculous or not; and a way was opened for the prevention of the disease by barring the way to the entrance of the bacillus into the human or other organism.

Koch's researches naturally excited fresh and renewed investigations on the part of others as well as of himself; rapid advances were made in our knowledge of the bacillus, and the technical methods of ascertaining its presence, recognising its characters and securing adequate cultures, were speedily developed.

For some considerable time the bacillus giving rise to the disease was considered both by Koch himself and by others to be the same organism, whether the disease occurred in man or in any other of the animals subject to it. After a while, however, the inquiries of many observers, especially those of Straus and Gamaleia in 1891 made it clear that the tuberculosis of fowls and other birds differed from that of mammals. The bacillus of avian tuberculosis was found to be unlike that of mammalian tuberculosis in many of its microscopic characters, in its cultural features, and especially in its effects when introduced into the bodies of animals. Thus, whereas the bacillus of the tuberculosis of man or of the ox readily produced tuberculosis when injected into the bodies of guinea-pigs even in very small doses, the bacillus of avian tuberculosis failed to do so even in very large doses; and other similar discrepancies were observed. Hence the bacillus of avian tuberculosis came to be recognised as an organism distinct from the bacillus of mammalian tuberculosis.

The bacillus of tuberculosis being studied not only from a microscopical but also from a chemical point, it was soon ascertained that the bacillus, in the course of the physiological processes attendant on its growth and multiplication, gave rise to various chemical substances, some of which had a toxic, poisonous effect when introduced into the bodies of animals. And it became recognised that the excretion of these toxic substances by the bacillus while it was setting up tuberculous processes in the body which it had invaded, played a not unimportant part in the development of the disease.

These chemical products of the bacillus, toxic and other, were found to be present in artificial cultures of the bacillus, being chiefly at least retained in the bodies of the bacilli and capable of being extracted from these in the form of a solution by the appropriate use of glycerin and other reagents. To such a more or less purified solution of these products the name *tuberculin* was subsequently given.

Koch was at first led to believe that the action of tuberculin, that is to say, of some or other of the products contained in the mixture called tuberculin, was antagonistic to the pathogenic activity of the bacillus, that if introduced into a body suffering from tuberculosis, it would arrest or even cure the disease. In this he proved to be mistaken; but the various observations on the effects of the administration of tuberculin brought to light this remarkable fact that a dose of tuberculin which has little or no effect on a healthy body, produces a marked reaction, a disturbance marked among other symptoms by a distinct rise of temperature, when given to the same body suffering from tuberculosis. So clear and precise are these results that tuberculin has come into common use, as a test for the presence of tuberculosis. If a certain dose (the dose differs with different animals) of properly prepared tuberculin be injected subcutaneously into the body of an animal (or of a man) a subsequent marked rise of temperature may be accepted as a proof that the animal is suffering from tuberculosis.

Although as stated above the bacillus of avian tuberculosis was early recognised as distinct from that of mammalian tuberculosis, the latter continued to be regarded, at least by most observers, as the same in all kinds of mammals. The bacillus of human tuberculosis was, for instance, considered as identical with the bacillus of bovine tuberculosis. At the International Medical Congress held in London in 1900, Koch brought forward the view that bovine and human tuberculosis were quite distinct. He asserted, as the result of his experiments and inquiries that the bacillus of human tuberculosis was unable to give rise to tuberculosis in the ox, and maintained that bovine tuberculosis could not be the cause of tuberculosis in man.

MEMORANDUM ON THE RESULTS OF THE EXPERIMENTS UP TO NOVEMBER 14TH, 1906.

I.

EXPERIMENTS WITH TUBERCULOUS VIRUSES OF BOVINE ORIGIN.

I. Origin of the Different Strains of Bovine Viruses.

The viruses used in the investigations are thirty in number (Viruses B. I. to XXX.), and include all those with which experiments have been performed. A complete record of the extent of the tuberculous lesions of the animals from which the viruses were obtained was not possible, as most of the material was obtained from the slaughter-house, but as far as could be ascertained, the cases of bovine tuberculosis may be considered as fairly typical of the chronic tuberculosis which occurs naturally in bovines. The material used for investigation included tuberculous lesions of the thoracic glands, lungs and pleuræ, mesenteric glands and bronchial glands. Many of the animals from which these lesions were obtained were in good general condition when killed, the lesions present being calcareous, and not extensive.

With these lesions in five of the viruses emulsions were made and injected into animals; and from all the viruses cultures were obtained, either directly from the original material, or from the lesions in a guinea-pig, rabbit or bovine, which had been inoculated with the original material. The cultures so obtained were used for inoculation and feeding experiments. The experimental results may be considered under the following headings:—(1) Character of the cultures obtained; (2) Effects of inoculation and feeding in Bovines; (*a*) In the form of emulsions, (*b*) In the form of culture; (3) Effect of inoculation and feeding in rabbits and guinea-pigs; (4) Effects of inoculation into, and feeding of, other animals than the above.

1. Character of the Cultures Obtained.

Dr. Griffith finds that an egg medium is of the greatest service in obtaining primary cultures of the bacillus. Cultures were obtained in the case of all the viruses, and were subjected to a continuous study, both by Dr. Griffith and Dr. Eastwood. They both agree that all the bacilli of bovine tuberculosis can be divided into three groups according to their mode of growth. They all grow on serum, and the characters of the growth are the same for all viruses, a uniform grey layer being formed at the end of the first week, increasing until the third week, when the growth apparently ceases. By the growth on glycerin media the viruses can be differentiated into three grades.

In Grade I. on glycerin serum no growth is observed till the second or third week, when discrete colonies appear, and at the end of six weeks the growth may be equal to that on pure serum. This grade is characterised therefore by the initial delay of the growth on glycerin serum. To it belong thirteen viruses, viz., B. I., B. III., B. IV., B. VI., B. XII., B. XIII., B. XV., B. XVII., B. XVIII., B. XIX., B. XXI., XXIV., B. XXVI.

In Grade II. the growth on glycerin serum from the outset, and up to the end of the second week, is similar in appearance to that on serum alone and about equal in amount, the final amount of growth varying to some extent with the different viruses. To this grade belong eleven viruses, viz., B. II., B. VII., B. VIII., B. XIV., B. XVI., B. XX., B. XXII., B. XXIII., B. XXVII., B. XXIX. and B. XXX.

In Grade III. the growth during the first week on glycerin serum is more abundant than on pure serum, and progressively increases until it becomes at the end of the fourth week two or four times greater than on serum. To this grade belong six viruses, B. V., B. IX., B. X., B. XI., B. XXV., and B. XXVIII., the latter growing rather less well than the others.

The results on glycerin-agar and glycerinated potato agree with those obtained from growing the bacillus on glycerin serum.

The question of the stability of the bacillus in culture is discussed on page 68.

2. THE EFFECT OF INOCULATION AND FEEDING IN BOVINES.

(A) *Inoculation into Bovines.*

Inoculation of Emulsions.

(a) *Subcutaneous Injections.*—Injections of emulsions of the tuberculous lesions were made with only five viruses, Viruses B. I. to B. V. Both calves and adult bovines were used, and the general result is shown in the following Table. In the earliest experiments the number of tubercle bacilli was not estimated; in the later experiments they were counted.

SUBCUTANEOUS INJECTION OF EMULSIONS INTO BOVINES.

Dose of T.B.	Number of Calves.	Result.*		Number of Adult Bovines.	Result.	
		G.T.	A. B. C. D.		G. T.	A. B. C. D.
Not estimated - -	2	1	D.	4	3	D.
No T.B. found - -	2	1	C.	—	—	—
1,330 to 9,000	4	2	C. D.	2	2	—
110,000 to 205,000 - -	5	4	A.	1	—	B.
932,300 to 4·5 million	6	5	D.	2	—	C. D.
11·1 million to 14·6 million - - -	4	3	D.	—	—	—
542 million - -	1	1	—	—	—	—
Total - -	24	17	7	9	5	4

If the results are tabulated according to the viruses, the following is found:—

Virus.	Number of Calves.	Result.*		Number of Adult Bovines.	Result.	
		G.T	A. B. C. D.		G. T.	A. B. C. D.
Virus B.I. - - -	9	7	C. D.	3	1	B. D.
„ B.II. - - -	6	4	A. C.	4	4	—
„ B.III. - -	2	2	—	—	—	—
„ B.IV. - -	6	3	D. (3)	—	—	—
„ B.V. - - -	1	1	—	2	—	C. D.
Total - - -	24	17	7	9	5	4

* The explanation of the abbreviations used is as follows. They refer only to subcutaneous inoculations throughout the Report:—

G.T.—General Tuberculosis.
A.—Local lesion only.
B.—Local lesion and extension of the disease to the nearest lymphatic glands.
C.—Besides B, extension to glands beyond the nearest.
D.—The same as C, with a few calcareous lesions in some organs, or grey tubercles, that is a light dissemination of the disease, with evident incapacity to progress.

The smallest dose in a calf which produced disseminated lesions, although they were calcareous, was with Virus B. I., an emulsion of pig lesions, in which no tubercle bacilli were found on microscopic examination (Calf 104). The largest dose given, 542,000,000 odd, was in an emulsion of guinea-pig lesions, Virus B. II. (C. 160), producing widely disseminated tuberculosis, partly calcareous, and causing illness; the disease, however, not being so acute as in C. 124 (*see* below).

Of the calves that received a known dose, six either died or were killed when dying or ill, and the others were killed in good health.

None of the adult animals that received a known dose of tubercle bacilli died from the disease, and they were killed in periods of from 62 to 148 days.

Some consideration is necessary in regard to the effects of tissue emulsions, as these have been so extensively used for inoculations in the case of viruses of human origin.

Six calves showed only a slight degree of tuberculosis. The largest dose which produced a slight lesion was 11,000,000 odd tubercle bacilli of the original material of Virus B. IV. injected into Calf 118. The animal was killed 100 days after inoculation, and showed a local calcareo-caseous lesion, with calcareous tubercles in the lung and thoracic glands, and one each in the liver and spleen. Calf 120, injected with the same dose, showed, in the same time, a more generalised tuberculosis, still of a caseo-calcareous type. Other examples occur of the same kind, such as Calves 104 and 106, Virus B. I.; Calves 130 and 124, also of Virus B. I. In this latter case each animal received 9,000 tubercle bacilli. One was killed when well in 104 days, and showed sparsely disseminated calcareous tubercles; the other died in 71 days, and showed acute general tuberculosis.

Such instances as these show an irregular effect of the injection of tissue emulsions, an effect which cannot solely be ascribed to a number of bacilli being dead, because in the case, for example, of Calves 124 and 130. which received the same dose of the same emulsion, it is unlikely that one calf received so large a proportion of dead bacilli as to produce a small amount of disease, and the other received such a large proportion of living bacilli as to produce general tuberculosis. Both calves were of the same age, and it seems likely that the result is more correctly to be ascribed to the varying resistance of the calves to the disease than to any other condition. It is quite possible that the number of living bacilli varies considerably, say as between an old calcareo-caseous lesion and a lesion of acute tuberculosis in the bovine, but there is no accurate method of gauging this.

The general conclusion to be drawn from the subcutaneous injection of emulsions of bovine tuberculous lesions is that in the large proportion of cases the injection leads to a disseminated tuberculosis in the bovine, the lesions of which sometimes tend to retrogress, but at other times progress to death.

The animals included in the above Table comprise all those which were injected with tissue emulsions subcutaneously, whether from the original material or from lesions from animals in the passage experiments. With a view of comparing the results with the experiments performed with the viruses of human origin, the effects of the injection of emulsions of the original material may be shortly considered.

Emulsions of Original Material Injected into Bovines.—This was done with only four Viruses. (In Virus B. I. a culture from guinea-pigs' organs was at first used, and not an emulsion of the original material.) Five calves were injected. In two of these the dose was not estimated. Both showed slight generalised tuberculosis, and lived 92 and 118 days.

One calf received 4·5 million and two calves received each 14·6 million tubercle bacilli. The first calf showed generalised calcareous tuberculosis, and the other two much the same lesions after living from 78 to 145 days.

Two adult bovines received a dose of tissue emulsion, the number of tubercle bacilli in which was not estimated. One developed acute tuberculosis, and the other had a similar condition, only not so acute.

Two adult bovines received 4·5 million tubercle bacilli in tissue emulsion. One showed only a local lesion, and calcereous tubercles in the nearest gland, living 140 days. The other in 62 days showed a small local lesion and a few foci in the internal organs.

It is quite clear from these results that it is impossible to determine the degree of virulence of the tubercle bacillus in a bovine lesion by a single injection of emulsions made from tissues. The doses of bacilli which were given in tissue emulsions were of course infinitely smaller than the doses of culture which were given.

(b) *Intraperitoneal Injections.*—Only one intraperitoneal injection of an emulsion was made into calves: an emulsion of Virus II., containing about 205,000 tubercle bacilli. The animal was killed in 188 days, and showed chronic tuberculous peritonitis, with calcareous foci in the abdominal glands and in a few of the thoracic glands.

(c) *Intramammary Injections.*—Ten cows, six of which had calves sucking, were injected into two quarters of the udder with Viruses B. I., B. II., B. III. and B. IV. Two of these died and eight were killed. Of these eight, six were in a dying condition, and the other two appeared to be in good health. All the intramammary inoculations produced tuberculosis of the udder and neighbouring glands, and in seven of the cases the disease had become generalised. In only four of the cases was the number of tubercle bacilli injected into each quarter calculated, and in two of these, Cows 44 and 64, the results were interesting.

Cow 44, injected with 1,000,000 tubercle bacilli in each of two quarters, died in forty-one days, but was found to have only local tuberculosis of the udder and neighbouring glands.

Cow 64 was inoculated from this cow with an emulsion of udder, 500,000 tubercle bacilli being injected into each quarter. It therefore received half the dose of Cow 44, and died in forty-eight days with tuberculosis of the udder, and dissemination of the disease throughout the body.

II. INOCULATION OF CULTURES INTO BOVINES.

Culture Inoculation into Bovines.

Twenty of the viruses were investigated by the inoculation of cultures into bovines (Viruses B. I. to B. XVIII., B. XXIII. and B. XXIV.). The total age of the cultures varied considerably, from 71 to 1,002 days, the total age being reckoned as the time the bacillus had been in culture or subculture. The generation of the cultures varied between the fifth and the eighteenth generation. The age of the culture injected was usually about three weeks. The cultures were injected subcutaneously in varying doses, two calves being inoculated at the same time with the same virus.

1. *Subcutaneous Inoculation of Culture in 50-milligramme Doses.*—Eighteen viruses were used (B. I. to B. XVIII.). Of the thirty-six bovines inoculated thirty-five were calves, and of these thirty-three died or were killed when very ill in 14 to 47 days. Two calves and one bull were killed in about 50 days, in apparent good health. All the animals showed lesions of generalised tuberculosis. The thirty-three calves that either died or became very ill showed tuberculosis in its acutest form, as was evidenced by a very large tuberculous mass at the seat of inoculation, and by caseation of the glands near the local lesion, and caseo-miliary tuberculosis of the lungs, liver, spleen, kidneys and suprarenal capsules, as well as caseation and caseous nodules in most, if not all, the lymphatic glands of the body, including the abdominal lymphatic glands.

2. *Subcutaneous Inoculation of doses of* 25 *milligrammes* in two calves (Virus B. VI. and B. X.), and of 12·5 *milligrammes* in one calf (Virus B. IV.), and 5 *milligrammes* (Virus B. XVI.) in one calf, produced general tuberculosis.

3. *Ten-milligramme Doses.*—Twelve calves were inoculated subcutaneously with doses of 10 milligrammes (Viruses B. V., B. IX., B. XVIII., B. XXIII., B. XXIV.) in order to determine whether there was any variation in the virulence. Eight of these calves died in 33 to 53 days with general tuberculosis. Four were killed in about 90 days in apparent good health. These calves were inoculated, one with Virus B. V., one with Virus B. XVIII., and two with Virus B. XXIV. Three of these calves had disseminated calcareo-caseous tuberculous lesions, showing that although the disease produced was not acute, yet it was progressing. One calf, however (Virus B. XVIII.), showed only a small amount of disease, somewhat resembling that produced by slightly virulent human viruses (see page 30). Thus in the calf there was a fibroid and caseous local lesion, scattered grey tubercles, some with calcareous centres, in the lungs, and a few scattered tubercles in the mediastinal glands, spleen and liver. It is to be noted that the other calves inoculated with 10 milligrammes of the same virus died of general tuberculosis, so that the result is probably to be ascribed to individual resistance on the part of the animal.

4. Still smaller doses were given in two calves. One calf received 0·02 milligramme subcutaneously (Virus B. III.). It was killed in good health 143 days after inoculation, and showed a small local lesion, with a caseous prescapular gland and a similar condition of the neighbouring lymphatic glands, a few calcareous tubercles in the liver and spleen, several in the lungs, and one or two tubercles in most of the lymphatic glands. Another calf received a dose of 0·01 milligramme subcutaneously (Virus B. V.) and was killed in 84 days in good health. It showed a small and chronic tuberculous mass at the seat of inoculation, a few caseo-calcareous tubercles in the prescapular gland, and no tuberculosis elsewhere in the body.

3. RESULTS OF FEEDING EXPERIMENTS IN BOVINES.

Feeding Experiments.

Feeding experiments were done with sucking calves, in whose mothers tuberculosis of the udder had been produced. In these cases the dose of bacilli received by the calves could not be estimated. In other cases calves were fed with tuberculous milk, and in a third series of experiments calves were fed with a definite dose of culture of tubercle bacilli.

(A) *Tuberculosis in Calves Sucking their Mothers which had Tuberculous Udders.*

Six of these calves are to be considered (28, 86, 20, 50, 22, and 116).

Sucking Calves.

Calf 50, fed for 41 days, was killed in 151 days, and was found to have intestinal ulceration and general tuberculosis. This is the most severe case of tuberculosis in a sucking calf. It was fed with milk from a cow (500) which had disease of the udder, but not general tuberculosis.

In all the other calves there were lesions of the mucous membrane of the intestine, which were in three cases nodular and calcareous; in one case there were, in addition, a few small ulcers. The mesenteric glands in all were affected with calcareo-caseous nodules, and two of the calves showed a few calcareous tubercles in the internal organs. In one case the submaxillary and pharyngeal glands were affected, as well as the intestinal. The calves were kept alive for a period ranging between 74 and 363 days.

The milk from all these cows produced tuberculosis in guinea-pigs, and the main result of feeding calves with this milk was disease localised in the intestine and neighbouring glands, the lesions in the glands being mainly calcareous.

It is of importance to note the localisation of the disease in most of these cases of prolonged natural feeding with tuberculous milk as showing the variety of tuberculosis obtained from the milk given in various degrees of infection of the udder.

(B) *Tuberculosis in Calves Fed with Tuberculous Milk and with Culture.*

The milk used was that given by cows with tuberculous udders.

Calves fed with Milk. 1st Series.

(1.) Six calves, each aged two months, received doses of bacilli in milk as follows:—Two received 1,000,000 each, two 5,000,000 each, and two 10,000,000 each.

Of those that received 1,000,000: one that was killed in sixty-four days showed only a pharyngeal gland extensively tuberculous; the other, killed in 98 days, showed slight tuberculosis of the intestine and the ileo-colic glands.

Of those that received 5,000,000: one, killed in 36 days, showed well marked tuberculosis of the intestine and mesenteric glands, and slight disease of the ileo-colic glands; the other, also killed in 36 days, showed well-marked tuberculosis of the intestine and mesenteric glands, and slight tuberculosis of the ileo-colic and colic glands. There was no visible tubercle in the spleen or thoracic glands, but emulsions of these parts caused tuberculosis in guinea-pigs.

Of the two that received 10 million: one, killed in 36 days, showed well-marked tuberculosis of the intestine and mesenteric glands, slight tuberculosis of the ileo-colic and colic glands; the gluteal gland was also affected. The other, killed in 96 days, showed the same extent of lesion, with affection also of the portal glands.

2nd Series.

(2.) Eight calves, varying in age between five and a half weeks and seven months, were fed, four with 1,000,000 tubercle bacilli each and four with about 10,000,000 each. They were killed in periods varying from 43 to 135 days. They all showed very slight tuberculosis, either in the intestine or intestinal glands or both, a few also in the liver and portal glands, and, in three cases, in the thoracic glands.

Calves fed with Culture.

Two calves were fed with culture from Virus B. IX., each receiving 1·0 milligramme.

One was killed in 50 days, and showed a few yellow foci in the tonsils, slight tuberculosis of the pharyngeal, mesenteric and ileo-colic glands, and two calcareous foci in the caudal mediastinal gland. The other was killed in 140 days; the tonsils were enlarged and tuberculous; there were numerous large sub-mucous caseating nodules in the stomach and extensive ulceration of the small intestine. The pharyngeal, cervical, gastric, mesenteric, ileo-colic, and coeliac glands were enlarged, dense and caseo-calcareous and in some cases softened. The spleen contained two yellow calcareous tubercles, the liver half a dozen nodules up to a pea in size, and the kidney three grey tubercles. In the lungs were moderately numerous dark red angular patches ranging up to 5 millimetres or more in diameter; some of these contained caseous foci or small gritty tubercles; others were homogeneous; besides these there were three or four firm yellow caseous gritty nodules ranging in size from a pea to a French bean. The bronchial and mediastinal glands were enlarged, dense, and caseating, and there was slight tuberculosis of the pleura and peritoneum.

4. EFFECTS OF INOCULATION INTO RABBITS AND GUINEA-PIGS.

Cultures and Emulsions.

(B.) *Inoculations into Rabbits.*—The virulence of each of the thirty viruses was tested in rabbits. The results of inoculating emulsions of tissues and definite doses of pure culture into rabbits intravenously, intraperitoneally and subcutaneously, is shown shortly in the following table:—

RABBITS INOCULATED WITH BOVINE VIRUSES.

EMULSIONS.	Number of Rabbits.	Duration of life in days.	Dose of T.B.	General Tuberculosis.	Slight Tuberculosis.	Died soon after injection.
Viruses—						
B. I., B. VI. - - - - - - (Intravenous.)	2	36 45	Not estimated	2	—	—
B. I., B. II., B. IV., B. V., B. IX., B. XI., B. XII., B. XIV., B. V., B. XVI., B. XVII., B. XVIII., B. XXVI., B. XXIX., B. XXX. (Intraperitoneal.)	19	26 to 124	50,000 (1) 1 million 1·4 M. (4) Not estimated (14).	16	—	3
B. I., B. III., B. IV., B. V., B. IX., B. XI., B. XII., B. XXIX. (Subcutaneous.)	12	62 to 142	50,000 (1) 1 million 1·4 M. (7) Not estimated (4)	12	—	—
	33	—	—	30	—	3
CULTURE.						
Viruses—						
(*a*) B. I., B. II., B. III., B. V. to B. VII., B. X., B. XI., B. XIV., B. XXVI., B. XXVIII., B. XXIX., B. XXX.	14	10 to 21	1·0 mg.	13	—	1
(*b*) B. I. to XV., B. XVII., B. XIX. to B. XXX. (Intravenous.)	14	11 to 34	0·1 mg.	48	—	2
(*a*) B. II., B. III., B. V. to B. XXX.	60	11 to 38 60 to 63 150 (6)	1·0 mg.	60	—	—
(*b*) B. I, B. III. to B. XXVI., B. XXVIII. to B. XXX.	36	14 to 46 65 to 109 (3)	0·1 mg.	36	—	—
(*c*) B. XVIII. to B. XXVII. - (Intraperitoneal.)	11	25 to 65	0·01 mg.	8	—	3
(*a*) B. I. to B. XXV., B. XVII., to B. XXX.	49	38 to 114	1·0 mg.	47	—	2
(*b*) B. I. to B. VI., B. XV., B. XVI., B. XVIII. to B. XXVI., B. XXVIII., B. XXIX.	26	48 to 113	0·1 mg.	25	—	1
(*c*) B. XXVI. - - - - - (Subcutaneous.)	1	121	0·01 mg.	1	—	—
	247	—	—	238	—	9

It will be seen that, with emulsions, thirty-three rabbits were inoculated in one way or another with all the viruses except B. VII. and B. X., and B. XIX. to B. XXVIII. Thirty of these animals died of general tuberculosis; three died from accident or acute infection at too early a stage for the disease to develop.

A culture from each of the thirty viruses was injected into 247 rabbits intravenously, intraperitoneally or subcutaneously in doses of 1 milligramme, 0·1 milligramme or 0·01 milligramme. In 238 of these animals death was caused by generalised tuberculosis. In nine of these death occurred too early for the disease to develop.

Inoculation therefore of cultures of all the strains into rabbits produced an acute generalised disease which is very characteristic, terminating in an acute caseous tuberculosis of most of the glands and organs of the body.

The bacillus of bovine tuberculosis being so virulent for rabbits, two series of experiments were performed to determine if possible the limit of dose capable of producing generalised tuberculosis.

In the first series of experiments the estimation of the dose was not accurate enough for the experiments to be considered.

In the second experiment, however, the results are of interest. Six rabbits in all were inoculated, the first with a dose of 0·01 milligramme of a culture of Virus B. IV., the second with a hundredth that dose, the third with a ten thousandth, the fourth with a hundred thousandth, the fifth with a one millionth, and the sixth with one ten millionth. All the animals, with the exception of the two last, which received the smallest dose, developed general tuberculosis. The two exceptions showed no tuberculosis.

The rabbit must therefore be considered as very sensitive to the action of the bacillus of bovine tuberculosis.

Feeding.

Feeding Experiments in Rabbits.—Six rabbits were fed, each with 1 milligramme of culture. One died too early for the disease to develop, and the others were killed in from 48 to 121 days. One of these was healthy, the second showed general tuberculosis, the other three moderate or slight tuberculosis.

Three rabbits were fed with the tuberculous milk of Cow 164 (Virus B. IV.) for 6 days. One died in 6 days; the others became tuberculous.

Four rabbits were fed with the tuberculous milk of Cow 172 (Virus B. IV.) for 31 days; three became tuberculous; one was killed in 111 days and found healthy.

Thirteen rabbits were fed by catheter with single doses of tuberculous milk in doses of 10,000 to 1,000,000 tubercle bacilli. But the experiment must be discarded as a feeding experiment with doses in series, as some of the animals showed insufflation tuberculosis.

Guinea-pigs.

Inoculations into Guinea-Pigs.—Of each of twenty viruses 0·1 milligramme of culture was inoculated subcutaneously or intraperitoneally into guinea-pigs, and in all the animals general tuberculosis resulted.

Feeding Experiments in Guinea-Pigs.—Two guinea-pigs were fed with 0·1 milligramme of culture and ten with 1 milligramme of culture. All developed general tuberculosis except two, which showed only local tuberculosis. In all cases the mesenteric glands were affected, and in ten there were lesions in the small intestine.

Seventeen guinea-pigs were fed with single doses of the tuberculous milk of Cow 164 (Virus B. IV.): only four became tuberculous.

Three guinea-pigs were fed with the same milk for 6 days; all became tuberculous.

Eight were fed for 31 days with the tuberculous milk of Cow 172 (Virus B. IV.) three remained healthy, five became tuberculous.

III. Effects of Inoculation into and Feeding of other Animals than the above.

5. The Effect of the Viruses of Bovine Origin in Pigs from Inoculation and Feeding.

(A) *Inoculation.*

Pigs. Inoculation.

Virus B. I.—One pig was inoculated subcutaneously with 0·1 milligramme of culture of Virus B. I. It was killed in 240 days and showed a small local lesion: caseation of the nearest glands: sparsely scattered hard tubercles in the lungs: three tubercles in the spleen and numerous tubercles in the liver. The thoracic and portal glands and one lumbar gland were caseous throughout; several other glands showed slight tuberculosis. A generalised but chronic disease was therefore produced.

Another pig was inoculated with 1 milligramme of the same culture, and died in 78 days of general tuberculosis.

With Virus B. I. four other inoculation experiments were performed.

Two pigs (10 and 12) were inoculated with an emulsion of the mesenteric glands of Pig 8, which had been fed with the tuberculous milk of Cow 40. No tubercle bacilli were found in the emulsion used for inoculation. Both pigs showed generalised tuberculosis when killed in about 120 days.

From one of these animals an emulsion of the lesions was obtained, and inoculated into two other pigs (14 and 16), the number of bacilli inoculated being estimated at 9,000. Both animals were killed in over 100 days and showed generalised tuberculosis.

Virus B. IV.—One milligramme of the culture of this virus, inoculated subcutaneously into a pig, caused general tuberculosis.

Virus B. IX.—One milligramme injected subcutaneously in a pig caused general tuberculosis, the lungs being severely affected. The pig was killed when very ill, 92 days after inoculation.

Virus B. XXVIII.—Three pigs were inoculated subcutaneously with doses of 10 milligramme, 1 milligramme, and 0·1 milligramme. The one that received 1 milligramme died in 48 days of general tuberculosis. The others were killed in 81 and 83 days and showed generalised tuberculosis, not severe.

(B) *Feeding Experiments.*

Feeding with Tuberculous Milk.

(1.) Two pigs (2 and 4) were fed with the tuberculous milk of Cows 500, 4 and 18 (Viruses B. I. and B. II.) for 21 days. One killed in 160 days showed ulcers in the small intestine, tuberculosis of the pharyngeal glands and tonsils and of the mesenteric glands, and extensive tuberculosis of all the organs of the body. The other pig killed in 264 days showed no lesion in the tonsils or pharyngeal glands, no ulceration of the intestine, but great enlargement and caseation of the mesenteric glands, and extensive tuberculosis of the internal organs of the body. Both animals showed the typical generalised disease from feeding with large doses. The difference in the intestinal lesion in the two animals is particularly to be noted.

(2.) Two pigs were fed for 92 days with the tuberculous milk of Cow 40 (Virus B. I.). They were killed in 99 days. Both showed generalised tuberculosis; in both the mesenteric glands were greatly affected, and there were disseminated lesions in the organs of the body. In one the intestine was normal; in the other there were two small nodules in the jejunum.

With 10,000,000 bacilli.

(3.) One pig was fed with a dose of tuberculous milk of Cow 172 (Virus B. IV.) containing 10,000,000 bacilli. It was killed when dying in 137 days, and showed ulceration of the tonsils, tuberculosis of the neighbouring glands, no ulceration of the intestine, and a few tubercles in the mesenteric glands, and extensive tuberculosis of the internal organs and lymphatic glands other than those mentioned.

With 1,000,000 5,000,000 10,000,000 bacilli.

(4.) Twelve pigs, six ten weeks old, and six seven to nine months old, were fed with different doses of the milk of Cow 64 (Virus B. I.). The milk from the infected quarters of this animal produced tuberculosis by inoculation in guinea-pigs. In the pig experiments each individual of each pair of pigs (one young and one old) received 1,000,000, 5,000,000 and 10,000,000 tubercle bacilli. The pigs were killed in periods of between 39 and 117 days. The results show that the young animals developed more tuberculosis than the older ones, that speaking generally those that lived longest showed the most tuberculosis (with doses of 5,000,000 and 10,000,000 more particularly), and that two animals, both young ones, showed general tuberculosis at death. All the animals became tuberculous.

With 1,000,000 bacilli.

(5.) Two young pigs and two adult pigs were fed each with 1,000,000 tubercle bacilli. One young pig, killed in 42 days, showed slight disease of the submaxillary and pharyngeal glands, of the liver and lungs. The other young pig, killed in 89 days, showed slight tuberculosis of the tonsils, well marked tuberculosis of the submaxillary glands, of the liver and lungs, while there was slight disease of some of the abdominal lymphatic glands, of the thoracic glands, the peritoneum and pleura; a generalised disease resulted, therefore, most marked in the submaxillary glands, in the liver and lungs. One adult pig, killed in 42 days, showed only slight disease of the ileo-colic glands; the other, killed in 90 days, showed slight disease of the ileo-colic glands, the portal glands and the liver.

(6.) One young pig and one adult each received about 1,000,000 tubercle bacilli, and were killed in 131 and 132 days. The young pig showed general tuberculosis, most marked in the submaxillary glands, the pharyngeal and cervical glands, the liver and portal glands, the thoracic glands, peritoneum and pleura. The adult pig showed only slight disease of the mesenteric glands and the portal glands.

With 100,000 bacilli.

(7.) Two young pigs and two adult pigs were fed with 100,000 tubercle bacilli. One young pig, killed in 42 days, showed no disease; the other, killed in 49 days, showed tuberculosis of the submaxillary glands, of the spleen, kidneys, well marked disease of the lungs, and slight disease of the thoracic glands and pleura. The two adult pigs, killed in 43 and 51 days, showed slight disease of the mesenteric and ileo-colic glands.

With 10,000 bacilli.

(8.) In a second series, pigs were fed with the milk of Cows 164 and 172 (Virus B. IV.). Four young pigs and two adult pigs received 10,000 tubercle bacilli each. One died in 8 days, too early for any disease to develop. Two of the young pigs were killed in 26 and 48 days, and showed no tuberculous lesion. One was killed in 131 days, and showed no disease; one adult pig was killed in 43 days, and showed slight tuberculosis of the mesenteric glands: and the last adult pig was killed in 120 days, and showed slight disease of the ileo-colic glands.

The series of experiments of feeding pigs with varying doses of tubercle bacilli is interesting as showing the anatomical distribution of lesions of tuberculosis occurring from feeding. These animals, as well as the calves, demonstrate the occurrence of general tuberculosis from feeding.

Anatomically it is interesting to note in Pig 54, an animal four weeks old fed with 100,000 bacilli, the slight disease of the submaxillary glands, and most marked disease of the lungs.

Feeding with Culture.

(9.) *Feeding with Culture.*—One pig was fed with 10 milligrammes of culture (Virus B. XXVII.). It was killed in 104 days and showed generalized tuberculosis. Two young pigs and two adult pigs were fed each with 1 milligramme of culture. One young and one old were killed in forty-eight days. Both showed generalized tuberculosis, more extensive in the young pig than in the adult. The other two were killed in over 100 days, and the young pig showed generalised tuberculosis, while the adult was less severely affected, and the disease was retrogressing.

Another pig fed with 1 milligramme (Virus B. XXVIII.) was killed in 109 days and showed generalized tuberculosis.

One young pig, fed with 0·1 milligramme of culture, was killed in over 100 days, and showed general tuberculosis.

General Results.—The pig is therefore very susceptible to infection by the bacillus of bovine tuberculosis, both by inoculation and by feeding.

The Effect of the Viruses of Bovine Origin in Goats by Inoculation and Feeding.

(A) *Inoculation.*

Goats. Inoculation.

An adult goat was inoculated subcutaneously with an emulsion containing 5,000 tubercle bacilli, obtained from the calf in the last passage in Virus B. II. It was killed in 161 days, and showed disseminated tuberculosis, not acute.

Another animal, inoculated with the same stock of emulsion, containing 4·4 million tubercle bacilli, was killed in 165 days, and showed general tuberculosis.

With Virus B. V. an adult goat was inoculated subcutaneously with the emulsion of the original material, containing 4·5 million tubercle bacilli, and died in 54 days from general tuberculosis.

Another animal was inoculated subcutaneously with 0·01 milligramme of the culture of the same virus. It died in 91 days of general tuberculosis.

(B) *Feeding Experiments.*

Feeding with Milk.

Eight goats were used for feeding with the milk of Cows 164 and 172 (Virus B. IV.).

Two young goats received 1,000,000 tubercle bacilli. One was killed after 44 days, and showed slight disease of the mesenteric glands. The other was killed in 130 days, and showed slight disease of the mesenteric and gastric glands, the liver, portal glands, lungs and mediastinal glands. Of two adult goats which received the same dose one was killed in 44 days, and showed no lesion. The other was killed in 129 days, and showed slight disease of the pharyngeal glands, of the liver, bronchial glands and mediastinal glands.

The disease resulting, therefore, from this small dose in goats was slight.

Two young goats and two adult each received 10·15 million tubercle bacilli. One young goat killed in 45 days, showed slight tuberculosis of the gastric glands only. A second young goat, killed in 132 days, showed marked tuberculosis of the tonsils and of the lungs, and also of the stomach, and slight tuberculosis of the glands in connection with the tonsils and the neck, and also of the spleen and liver. Of the adult goats which received the same dose, one was killed in 45 days, and showed slight tuberculosis of the gastric glands, and the other was killed in 133 days, and showed tuberculosis of the pharyngeal and gastric glands.

Only one animal of the series therefore developed generalised tuberculosis, and that was a young goat that received 10,000,000 bacilli.

Feeding with Culture.

Two goats, one young and one adult, were fed each with 1 milligramme of culture, and killed in over 100 days. Both showed a limited extent of disease in the glands in connection with the alimentary tract. In the adult goat the internal organs were not tuberculous. In the young goat there was one nodule in the lung. The disease was not only limited, but appeared to be arrested.

General Results.—Goats are very susceptible to inoculation in small doses of the bacillus of bovine tuberculosis, but to feeding with the bacillus they are apparently less susceptible than pigs.

EFFECT OF THE BOVINE VIRUS IN MONKEYS (RHESUS AND BABOONS) AND LEMURS.

(A) *Inoculation.*

Monkeys. Inoculation.

The monkeys inoculated with the emulsion of Virus B. I., in which the dose was not estimated, were Rhesus, and the experiments had to be discarded owing to the occurrence of spontaneous tuberculosis in the animals, the disease having been already present in the animals when they arrived at the farm.

Three other Rhesus monkeys, inoculated subcutaneously with the emulsion of Virus B. I., all showed general tuberculosis, and died in about 43 days. One, inoculated intravenously, showed general tuberculosis in 15 days, and another, inoculated intravenously, died in 9 days, showing tubercle bacilli in all the organs, but no tuberculous lesion.

Two baboons were subcutaneously inoculated with a culture from Virus B. IV. One died in 3 days, and the other, receiving a 1-milligramme dose, died in 49 days with generalised tuberculosis, not extremely acute.

With Virus B. XXVI. four monkeys were inoculated subcutaneously with doses of 10 milligrammes, 1, 0·1, and 0·001 milligramme of culture. The monkeys inoculated with 10 milligrammes, 1 and 0·001 milligrammes died of general tuberculosis in 35, 45 and 45 days respectively; that inoculated with 0·1 milligramme was killed when very ill in 56 days and showed general tuberculosis.

(B) *Feeding.*

Feeding Rhesus with Tuberculous Milk.

Three Rhesus monkeys were fed with the milk of cow 74 (Virus B. I.), in which the dose of tubercle bacilli was not estimated. One animal, fed only once, showed no lesion in 20 days. Another animal, fed for 5 days, was killed in 24 days, and showed generalised tuberculosis. A third young animal was fed for 66 days, and killed in 77 days. This showed acute tuberculosis, chiefly thoracic. It was discussed in this case whether the tuberculosis of the lungs arose from infection by way of the alimentary tract, or whether it was due to insufflation. No definite conclusion can as yet be arrived at on this point from this or any of the experiments.

Two Rhesus monkeys were fed with the milk of cow 68 (Virus B. III.) for 33 days. Both were killed in 87 days. Both showed ulceration of the caecum, with abdominal tuberculosis, and a slighter degree of tuberculosis in the thoracic organs, but whereas in one the abdominal tuberculosis showed itself chiefly as tuberculous peritonitis, in the other the tuberculosis was glandular.

With Culture.

One Rhesus monkey, fed six times with culture of Virus B. III., dose not estimated, died in 40 days. It showed tuberculosis of the intestine and of the mesenteric glands, and the post-pharyngeal and cervical glands, and slight tuberculosis of the lungs.

These three experiments are interesting as showing the production of general tuberculosis in monkeys from feeding with comparatively large doses of the bovine bacillus.

With 100,000 and 1,000,000 Bacilli.

Eight Rhesus monkeys, four adult and four baby, were fed with tuberculous milk of cows 164 and 172. Two adults and two baby monkeys each received 100,000 tubercle bacilli. Two were kept alive 42 days and the others 120 days.

Two adult and two baby monkeys each received 1,000,000 bacilli. Two were kept alive 42 days, and the others 120 days. Only one animal showed a tuberculous lesion, a few small nodules in the liver. All the other animals were normal.

It is difficult to explain these experiments on the supposition that these animals were given living tubercle bacilli.

Baboons fed with Tuberculous Milk.

Five baboons were fed with the milk of Cow 172 (Virus B. IV.). One died too early for tuberculosis to develop. The others, two young and two adult, were fed for 25 days with a total quantity of 2,000 cubic centimetres of milk. One young baboon died in 30 days, showing slight caseous tuberculosis of the submaxillary, retro-pharyngeal, ileo-colic, and coeliac glands, nodules in the spleen, left tuberculous purulent pleurisy, and caseation in the thoracic glands. There was no lesion in the intestinal tract.

The second young baboon died in 80 days, and showed intestinal tuberculosis and ulceration, extensive tuberculosis of the glands connected with the intestine, and to a less extent of the spleen, liver, lungs and thoracic glands.

One adult baboon was killed when very ill in 85 days. The tonsils, stomach, and intestine showed tuberculous ulceration, with tuberculosis of the glands in connection, and general tuberculosis of all the organs.

The second adult baboon died in 90 days, and showed caseation of one tonsil, tuberculous ulceration of the stomach and intestine, tuberculosis of the glands attached to the alimentary tract, and general tuberculosis of the glands and organs of the body.

Six baboons, three young and three old, were fed with tuberculous milk from Cow 64, each pair, young and old, receiving 1,000,000, 5,000,000, 10,000,000 tubercle bacilli. In five of the cases the results are interesting, as showing the spread of tuberculosis from feeding with known doses, one of these animals showing an extensive tuberculosis. One of the young baboons showed spontaneous lung tuberculosis, and the series of experiments was therefore not of great value.

With Culture. One milligramme.

Three baboons were fed with one milligramme of culture of Virus B. IV.

One young baboon died in 37 days, and showed intestinal ulceration, and tuberculosis of the submaxillary, pharyngeal, and mesenteric glands, the other organs of the body being normal.

Of the two other baboons, one young and one old, the young one died in 74 days, and showed ulceration of the tonsils and intestine, tuberculosis of the glands attached, and general tuberculosis.

The adult baboon was killed in good health in 77 days, and showed tuberculosis of the lungs, and of no part of the alimentary tract or the glands attached. This may possibly be a case of spontaneous tuberculosis, which developed also in another case, in which the baboons were fed with culture.

Seven monkeys (Rhesus, Mandrill, Baboons, and Mangabey) and two lemurs, received by feeding each one milligramme of culture of the bovine bacillus.

One of the monkeys died of ulcerative colitis; the others all developed generalised tuberculosis in an acute form, usually with affection of the intestines, and sometimes of the tonsils.

General Results.—The various species of monkeys and lemurs used are very sensitive to the action of the bacilli of bovine tuberculosis, both by inoculation and by feeding. The experiments clearly show this, even when allowance is made for the somewhat frequent occurrence of actual tuberculosis in monkeys kept in captivity.

EFFECT OF THE BOVINE VIRUS IN CHIMPANZEES.

(A) *Inoculation Experiments.*

Chimpanzees Inoculation.

One milligramme of culture of Virus B. IV. was inoculated subcutaneously into a chimpanzee. The animal died in 55 days, and showed a large local lesion and acute general tuberculosis of all the glands and organs of the body.

Another chimpanzee receiving 0·001 milligramme subcutaneously died in 87 days of general tuberculosis.

(B) *Feeding Experiments.*

Feeding with Tuberculous Milk.

(1) Two chimpanzees were fed with the tuberculous milk of Cow 172 (Virus B. IV.).

One, fed for one week, received 1,000 cc. of infected milk. The total number of tubercle bacilli was approximately estimated as 100,000,000. It was killed in 100 days, and showed numerous tuberculous ulcers in the small and large intestine, extensive tuberculosis of the glands attached to the intestine, and tuberculosis of the spleen and lungs.

The other chimpanzee received 107 cc. of the same milk, containing 10,000,000 tubercle bacilli. It died 144 days after being fed. The small intestine showed nine tuberculous ulcers, the mesenteric glands were fibro-caseo-calcareous. There was an abscess in the abdominal wall; the lungs showed pneumonia, but no tuberculous lesion.

With Culture.

2. (*a*) One chimpanzee received 1 milligramme of a culture of Virus B. IV. It was a young animal, and died in 56 days. It showed tuberculous ulceration of the small intestine, caseous tuberculosis of the mesenteric and colic glands, and a few tubercles in the spleen. There was extensive tuberculosis of the lungs.

(*b*) Four other chimpanzees were fed with culture. One, fed with 1·1 milligramme (Virus B. IX.), died of acute general tuberculosis; one, with 0·1 milligramme (Virus B. IV.), died of general tuberculosis; two with 0·01 milligramme (Virus B. IV. and B. IX.) died of acute general tuberculosis.

General Results.—The production of acute tuberculosis in chimpanzees by subcutaneous inoculation and by feeding with varying doses is thus clearly established.

EFFECT OF THE BOVINE VIRUS IN CATS.

(A) *Inoculation.*

Cats.

Three cats were subcutaneously inoculated with 1 milligramme of culture, two adults from Virus B. I., and a kitten from Virus B. III. The adult cats died respectively in 35 and 49 days of general tuberculosis. The kitten (Virus B. III.) died in 17 days, with a local lesion and affection of the nearest lymphatic glands, and tubercle bacilli were present in the spleen, liver, lungs, and marrow. Death apparently occurred too early for lesions to form in the internal organs.

One cat was inoculated subcutaneously with 1 milligramme of culture (Virus B. XVIII.). It died in seventy days, and showed only a moderate degree of disseminated tuberculosis.

A kitten inoculated with the same dose of the same virus died in 25 days of acute tuberculosis.

One cat and one kitten were inoculated intraperitoneally with one milligramme of culture of Virus B. III. The cat died in 39 days, and showed tuberculous peritonitis, with caseation of the abdominal glands, and a few tubercles in the lungs and liver. The kitten died in 17 days, and showed also tuberculous peritonitis and caseation of the abdominal glands and of the thoracic glands, the internal organs not being affected to any extent.

Two cats and three kittens were inoculated subcutaneously with a culture from Virus B. XXVIII. One of the cats, a young adult, inoculated with 0·1 milligramme, died in 22 days of acute tuberculosis, tubercle bacilli being very numerous in the marrow and all the organs; the other cat, older than the latter, inoculated with 1 milligramme was killed in 74 days in apparent good health: it showed a local ulcer, caseation of the nearest glands, and miliary tuberculosis of the lungs and kidneys.

The three kittens received 1·0, 0·1, 0·01 milligramme, and died in 21, 34, and 39 days, respectively, of acute disseminated tuberculosis, the lungs in each case being severely affected.

(B) *Feeding Experiments.*

Ten cats were fed either with tuberculous milk or with guinea-pig organs, five adults and five kittens. None of the animals died and none showed, when killed, extensive tuberculosis. The doses given were:—Two kittens received 1,000,000, two adults 1,000,000, and two kittens and two adults each 10·15 million tubercle bacilli. In two cases the dose was not estimated.

Two adult animals (1,000,000 and 10·15 million) showed no tuberculosis. They were killed in 43 and 46 days.

One kitten, with 10·15 million, showed two small ulcers in the intestine and slight tuberculosis of the mesenteric and ileo-colic glands.

The other six animals showed only minimal and calcareous lesions in the glands attached to the intestine or in the pharyngeal glands. One adult animal showed slight tuberculosis in the lungs.

Two adult cats and three kittens were fed each with 1 milligramme of culture. They were killed at periods varying from 47 to 121 days. In the adult cats tuberculosis of the mesenteric glands alone was present, while the three kittens showed tuberculosis of the pharyngeal, mesenteric, and ileo-colic glands, and one showed ulcers of the intestine, while in all the lungs were affected.

Two adult cats were fed each with 10 milligrammes of culture from Virus B. XXVI. One killed in 71 days showed only two small foci in a mesenteric gland and scattered miliary tubercles in the lungs; the other killed in 73 days showed more extensive disease, viz., tuberculosis of the tonsils, the pharyngeal, submaxillary, mesenteric and ileo-colic glands, the bronchial and portal glands; a caseous nodule in the spleen, and miliary tuberculosis of the lungs.

General Results.—The bacillus of bovine tuberculosis in cats can produce general tuberculosis by inoculation and feeding. Kittens are much more susceptible to the virus than adult cats.

EFFECT OF THE BOVINE VIRUS IN DOGS.

(A) *Inoculation Experiments.*

Dogs. A dog inoculated intraperitoneally with an emulsion of guinea-pigs' organs, containing 10·15 million tubercle bacilli, was killed when very ill in 71 days, and showed general tuberculosis.

At the same time and with the same dose another dog was inoculated subcutaneously. It was killed when well in 171 days and showed no tuberculosis, the local lesion having disappeared.

Two dogs were inoculated, one subcutaneously and one intraperitoneally with 1 milligramme of culture of Virus B. XXII. The one inoculated intraperitoneally showed only a few tubercles in the organs of the body. The one inoculated subcutaneously showed only a scar at the site of inoculation, and no tuberculosis.

Two puppies were inoculated, one subcutaneously, the other intraperitoneally, each with 1 milligramme of culture from Virus B. IX. The intraperitoneal animal died in 32 days and showed tuberculous peritonitis, early necrosis of the sternal and cœliac glands, a grey focus in each kidney, and several patches of broncho-pneumonia, but no tubercles in the lung. The subcutaneous animal was killed 98 days after inoculation, and showed a local lesion, tuberculosis of the nearest glands, and scattered tubercles in the lungs and liver.

An adult dog was inoculated subcutaneously with 10 milligrammes of culture derived from Dog 56, Virus B. IV. (*see* Appendix , Modification Experiments). and killed 76 days afterwards. At the seat of inoculation there was a small cavity with a sinus leading from it, a large tuberculous cavity in the region of one axilla and miliary tubercles of the fibrous variety in the lungs.

Two other dogs, one a puppy, the other an adult, were inoculated subcutaneously each with 25 milligrammes of culture from Virus B. XXIV., and killed in 92 and 93 days respectively. In the adult animal there was a small cavity at the site of inoculation, lined by granulation tissue, with two sinuses leading from it; the lungs contained a few minute grey tubercles, and there were a few doubtful foci in the liver and kidneys. The young animal also showed a tuberculous cavity at the site of inoculation, with several openings from it through the skin; the adjacent gland was tuberculous, and there was a sinus leading from it through the skin; there were about ten nodules in the lungs and numerous minute tubercles in the liver.

(B) *Feeding Experiments.*

Four adult dogs and four puppies were fed with tuberculous milk or emulsion of guinea-pigs' organs. Two adults and two puppies each received 1 million tubercle bacilli, and each of the others received 10·15 million. They were killed, four between 41 and 48 days, and four between 127 and 136 days. In only two animals were there any signs of any tuberculous lesion, and this was minimal.

Six dogs, three young and three adult, were fed each with one milligramme of culture. Two of the adult animals, when killed, were found free from tuberculosis; the third showed a doubtful lesion in the lungs. All the three young animals showed slight tuberculosis, in one case of the pharyngeal glands only, in another of the pharyngeal, mesenteric and bronchial glands, and of the tonsils and intestines; in the third case, of the pharyngeal, mesenteric and ileo-colic glands alone.

Ten dogs have been fed with culture; in six instances the culture used was derived from the original material of a bovine virus; in the remaining ones the culture had previously passed through a dog, or a series of dogs.

The doses varied from 1 to 100 milligrammes.

Three of the dogs, two fed with one milligramme, the other with 32·5 milligrammes, showed no sign of tuberculosis of any organ or gland.

Another fed with 25 milligrammes of a glycerine serum culture, and killed 64 days after, showed tuberculosis of one pharyngeal gland, and a few caseous nodules in the lungs.

In the other five dogs there was no disease of the alimentary tract or glands in connection with it, but, in each, one or two small tubercles in the lungs; these tubercles were of the fibrous variety, and were translucent throughout, except one (*see* Dog 102), which showed a fibro-caseous centre.

General Results.—Dogs are therefore very little susceptible to the bacillus of bovine tuberculosis, either by subcutaneous inoculation or feeding. They are more susceptible by intraperitoneal inoculation.

EFFECT OF THE BOVINE VIRUS IN RATS AND MICE.

(A) *Inoculation.*

Forty rats were inoculated, twenty-one subcutaneously and nineteen intraperitoneally, with cultures of tubercle bacilli from sixteen viruses. The dose was varied, but on an average was about 10 milligrammes. When subcutaneously inoculated rats are very refractory, no obvious disease being produced. With intraperitoneal injection, the animals may die, but as a rule there is no development of a tuberculous lesion in the body. Numerous tubercle bacilli are, however, found in the various organs. This dissemination of the bacilli occurs soon after inoculation. The results of inoculating the virulent bovine bacillus into rats are in great contrast to those obtained in other animals. **Rats.**

Fourteen mice were inoculated, 8 subcutaneously and 6 intraperitoneally, with an emulsion from the original material, Virus B. V., and with an emulsion from a gland of Calf 128, Virus B. I. The animals died in from 40 to 280 days, and showed in the main the same results as the rats, viz., a great multiplication of tubercle bacilli in the tissues without the formation of characteristic tuberculous lesions. In mice, however, unlike rats, thin walled nodules containing yellow pus full of bacilli are found in the peritoneal cavity, after intraperitoneal inoculation. **Mice.**

(B) *Feeding Experiments.*

Twenty-six rats were fed with tuberculous milk alone or with milk and tuberculous organs of rabbits and guinea-pigs for periods of from 12 to 33 days; so that they received an enormous dose of tubercle bacilli. In only two cases were any lesions found, and there were minute grey spots in the mesenteric glands containing tubercle bacilli. The rat therefore appears to be but little susceptible to tuberculosis by feeding. **Rats.**

EFFECT OF THE BOVINE VIRUS IN HEDGEHOGS.

(A) *Inoculation.*

Two hedgehogs were inoculated; one subcutaneously, with 50,000 tubercle bacilli in tuberculous milk, showed in 45 days a local lesion and caseation of the nearest glands. Another, inoculated with the same dose intraperitoneally, showed a moderate degree of general tuberculosis. **Hedgehogs.**

Two, inoculated subcutaneously with 1 milligramme of culture (Virus B. IX.), showed a local lesion, caseation of the nearest glands, and some dissemination in the organs of the body.

One, inoculated intraperitoneally with the same dose died in 19 days, showing a tuberculous peritonitis.

(B) *Feeding Experiments.*

Six hedgehogs were fed. Two were fed with an emulsion of tubercle bacilli, and showed no tuberculosis in 26 and 72 days.

Two were fed with tuberculous milk for 43 days; one killed in 43 days was healthy; the other showed tuberculosis in the cervical glands and left pharyngeal glands.

Two other hedgehogs were fed with tuberculous organs and milk; one showed in 55 days tuberculosis of the cervical and pharyngeal glands, and the other tuberculosis of one submaxillary gland.

Effect of the Bovine Virus in Mongooses.

(A) *Inoculation.*

Mongooses. One mongoose, inoculated subcutaneously with 1 milligramme of culture (Virus B. IX.), died in 29 days, showing a local lesion, with caseation of the nearest glands and a few lesions in the internal organs.

Another, inoculated intraperitoneally with the same dose, showed tuberculous peritonitis and a few tubercles in the spleen and abdominal glands.

In both animals bacilli were very numerous in the tissues.

(B) *Feeding Experiments.*

Four mongooses were fed each with 1 milligramme of culture, and died in from 21 to 59 days. Two showed no tuberculosis, one showed a caseous submaxillary gland and caseous bronchial glands, and the fourth showed tuberculosis of the submaxillary glands, pharyngeal mesenteric and ileo-colic glands, and of the spleen, liver, and lungs in varying degree.

THE QUESTION OF THE MODIFICATION OF THE BACILLUS OF BOVINE TUBERCULOSIS AS REGARDS CULTURAL CHARACTERS AND VIRULENCE, EITHER BY ARTIFICIAL CULTIVATION OR BY PASSAGE THROUGH ANIMALS.

1. Modification by Sub-Cultivation in Different Media.

The distinction between three grades of the bacilli of bovine tuberculosis has already been mentioned. By repeated sub-culture on glycerine media all viruses grow with increased luxuriance. This property is retained after passage through animals, such as the calf, rabbit, and guinea-pig, but the virulence of the culture is not diminished. (*See* Appendix .) It may therefore be concluded, from the large number of observations that have been made, that the bacillus of bovine tuberculosis only varies in cultural characteristics within somewhat narrow limits, even by prolonged sub-cultivation.

2. Modification by Passage through Animals.

Several series of experiments were performed to determine whether the bacillus became modified, either in cultural characteristics or in virulence, by passage through various animals. The animals used were the calf, pig, monkey and chimpanzee, the dog and the guinea-pig.

No modifications in cultural characters or in virulence were to be observed in passage through calves, pigs, guinea-pigs or chimpanzees.

Calf Passage. *Virus B. I.*—A passage was carried on from Cow 40 by an emulsion from a gland, in which a calf and two adult bovines received the same dose subcutaneously. Calf 102 developed generalised tuberculosis; the adult animals showed a less degree of disease (H. 28, H. 98). Here again there seemed only the difference between adult animals and young, and no difference in the characters of the bacillus.

From C. 102 the passage was continued into two calves in a small dose, and both of these developed general tuberculosis, and from one of these calves again intramammarily into one cow, and then into the mamma of another cow. But in considering this series there does not appear any difference in the virulence from Cow 40 to near the end, Cow 44, because a culture from Cow 40 and one from Cow 44 equally produced general tuberculosis in calves and rabbits in the large doses given.

Virus B. II.—A long passage experiment was undertaken with this virus from Cow 4; which had been injected intramammarily with an emulsion from the original material. From the mesenteric glands of the calf which sucked this cow an emulsion containing a small dose of bacilli (1,330) was injected into three animals, two adults and one calf (Sh. H. 100, H. 66, C. 114). There was generalised tuberculosis in all three. Subsequently from one of the adult animals an emulsion was injected into two calves in a dose of about 205,000 tubercle bacilli (C. 134, C. 136). In Calf 134 only a local lesion developed in 138 days. In the other calf (136) (intraperitoneal injection) there was local tuberculosis of the peritoneum and glands Here, without further experiment, one might consider that there was a diminution in the virulence, inasmuch as the doses in Calves 134 and 136 were fifteen times greater than that given in Calf 144 and Heifer 66. But it is to be noted that a culture from Heifer 66, with generalised tuberculosis, produced general tuberculosis in calves and rabbits, and a culture obtained from Calf 134, which showed only a local lesion, produced general tuberculosis in calves and rabbits.

To proceed with the passage. From Calf 134 the virus was passed through two sets of guinea-pigs, and an emulsion of the guinea-pigs' organs injected into four calves. Calf 158 (5,000 tubercle bacilli) developed only slight local tuberculosis. Calf 178, which received the same dose as Calf 134, had generalised tuberculosis. Calf 180, with 4·48 million tubercle bacilli, and Calf 160, with 542,000,000 tubercle bacilli, developed generalised tuberculosis.

It is quite evident from these results that with the bovine virus the production of a minimal lesion by a small number of tubercle bacilli is not to be taken as a sign of deficient virulence of the bacillus, as with a similar dose general tuberculosis may be produced. It may also be deduced that it is a more accurate gauge of the virulence of a strain of tuberculous virus to investigate the action of the culture in definite doses.

Virus B. IV.—Attention need only be called to the fact that a culture from the original material was highly virulent to calves and rabbits, and yet we have in Cows 172 and 164 the anomaly of the same estimated dose of tubercle bacilli, producing in one case (Cow 172) local tuberculosis, and in the other case death from generalised tuberculosis.

Virus B. V.—In Virus B. V. the only point to be noted in the passage, which was not carried out to any great extent, was that Calf 144, which received 4·5 million tubercle bacilli of a tissue emulsion subcutaneously, developed generalised tuberculosis, whereas Calf 202, which was rather older than Calf 144, and received 0·01 milligramme of culture, developed only local tuberculosis. 0·01 milligramme is supposed to contain at least 50 million tubercle bacilli, but in this case the emulsion containing a smaller number of bacilli appeared to be more virulent than the culture.

Other cases occurred in these experiments dealing with the point already mentioned, namely, that a small lesion, even though it be calcareous, produced by the bovine virus does not necessarily mean that a virulent culture cannot be obtained from it. This point need not be further elaborated. Suffice it to say that in experiments with calves injected with 50 milligrammes subcutaneously of culture in fifteen out of the twenty viruses the culture was obtained either from the original material direct or through guinea-pigs, and many of these lesions were old and calcareous.

Pig Passage.

Virus B. I. was passed through a series of four pigs in succession, all of which developed general tuberculosis. The total period of residence of the bacillus in the pig was 551 days. The culture obtained from the last pig of the series was unaltered, both in cultural characteristics and in virulence.

Chimpanzee Passage.

Virus B. IV. and *Virus B. IX.*—were passed through two series of chimpanzees. *Virus B. IV.* was used for feeding a chimpanzee, which died with tuberculous lesions. A culture from this animal was used for feeding a second chimpanzee, which died of tuberculosis, and a culture obtained from it was used for feeding a third chimpanzee. The total period of residence of the bacillus in the animal's body was 348 days.

A similar experiment was done with Virus B. IX., but no alteration in cultural characteristics or in virulence resulted from the passages.

Guinea-pig Passage.

Virus B. II. was passed through a series of twenty-four guinea-pigs by inoculation. The total period of residence in the guinea-pig's body was 3 years 166 days. The cultural characteristics remained precisely the same at the end, and the virulence was unaltered.

Monkey Passage.

Six Passage Experiments were carried out on monkeys and baboons with three viruses (B. I., B. IV., and B. IX.). In each experiment there were two passages, and with one exception the bacillus remained the same, both in virulence and in cultural characteristics. The exception was with Baboon 8, an animal which had been infected with the milk of Cow 64 (Virus B. I.). The culture showed a distinct increase in luxuriance on the differential media, and when passed into a second baboon showed a still further increase in luxuriance. The virulence, however, was unchanged.

A similar passage to the above was done with two lemurs but the bacillus was not altered in cultural characters or in virulence.

All the animals which have been mentioned, on which the Passage Experiments were done, were those that are highly susceptible to infection by the bacillus of bovine tuberculosis.

Dog Passage.

The dog possesses a high degree of resistance to the bacillus, and of the experiments performed up to the present it is not possible to decide definitely whether any modification of the bacillus occurs in the dog or not. All the animals were fed, Viruses B. IV., B. VIII., and B. IX. being used in individual experiments. From some of those that showed tuberculous lesions, Dogs 18, 50, 72 and 92, the cultures obtained were more luxuriant than the original culture. The virulence was unaltered except in the case of Dogs 18 (Virus B. IV.) and 50 (Virus B. IX.). These were non-virulent to rabbits. The experiments will have to be repeated before any conclusions can be drawn.

GENERAL REMARKS.

The following general conclusions are important in regard to the consideration of the results obtained with the viruses of bovine origin:—

1. Cultures of the bovine bacillus obtained from tuberculous lesions in cattle, whether from the original material or from lesions in animals inoculated with the original material, produce in calves, when given in fifty milligramme doses, general tuberculosis of all the organs and glands of the body, usually in a very acute form, and in the greater proportion of instances killing the animals, this occurring within a period of under 50 days. This dose must be considered an enormous one, as in view of the experiments done with smaller doses of culture, even five milligrammes has produced fatal general tuberculosis in a calf. In a series of calves injected each with ten milligrammes, one case occurred of minimal disease from the injection.

2. When injected into bovines in the form of emulsions of tuberculous lesions, the bovine virus in those strains that were tested (five in number) produces a generalised disease, but not in all cases, and instances are noted in which a minimal lesion was produced in a calf by the injection of an emulsion, and a virulent culture obtained from this lesion.

It is to be noted that the number of estimated bacilli injected in any of the animals is much smaller than that which is estimated to be contained in fifty milligrammes of culture, and the experiments make it quite clear that in estimating the virulence of any particular strain of virus for the bovine, it is not a sufficient test to use emulsions only for inoculation.

3. Injected into rabbits, cultures of the bovine tubercle bacillus produce general tuberculosis, either given subcutaneously or intraperitoneally, in doses of 0·1 and one milligramme. With rabbits, emulsions always produced general tuberculosis in whatever dose given.

4. With regard to the other animals used, general tuberculosis is produced by inoculation and feeding with the bovine virus in pigs, goats, and monkeys. Cats are susceptible by intraperitoneal and subcutaneous injection, and to a much less extent by feeding, and dogs are susceptible by intraperitoneal inoculation, but refractory by subcutaneous inoculation and feeding, while rats, mice, and hedgehogs are very insusceptible to feeding, rats being the most refractory.

5. It has also been clearly shown that the chimpanzee is highly susceptible to the bovine virus, both by inoculation and by feeding.

The results obtained by the bovine virus in these directions are so clear that it does not appear advisable to perform any more experiments on the same lines.

EXPERIMENTS WITH TUBERCULOUS VIRUSES OF HUMAN ORIGIN.

1. Origin of the Different Strains of Human Viruses.

The viruses used in the investigation were sixty in number (H. 1 to H. 66), and were obtained from human beings of all ages suffering from tuberculosis. Most of the material was obtained at the post-mortem examination of the cases. Some of the material, however, as, for example, that from cervical glands and joints, was obtained from operations on patients. A post-mortem record of the cases investigated, and a clinical record, as far as it was possible to obtain this, will be found in Appendix . For the purposes of this Memorandum the cases will be divided into classes according to the presumed seat of origin of the tuberculosis. The following classes of cases were examined:—

1. *Sputum* from cases of pulmonary tuberculosis (4 cases). Animals were fed with this, and cultures were obtained from the sputum and used for inoculation.

2. Lesions of the lung in cases of *primary pulmonary tuberculosis* were examined in ten cases. These are called primary lung tuberculosis, because they exhibited the features associated with that disease: tuberculosis of the lung, with destruction, being the main lesion in the body. Some of the cases had other tuberculous lesions in the body, which were secondary to the lung. In one case (H. 58, "F.G."), as the cervical glands had obviously been diseased, although no longer actively so, being hard and calcareous, the first tuberculous infection may have been in the cervical glands. The patient, however, died of active tuberculosis limited to the lungs. Eight of the patients in this class were adults over twenty-five years of age; two were aged sixteen and one year respectively.

3. In one case of *general tuberculosis* in a child the primary seat of disease was undiscoverable (H. 35, "C.B."). A good many other cases of general tuberculosis have been investigated, but in all these the origin of disease was either in the bronchial glands or in the mesenteric glands.

4. *Bronchial Gland Tuberculosis.*—Four of these cases were investigated. They occurred in children. In two the bronchial glands were the only parts tuberculous. In the others the disease had affected the lungs as well, in the form of miliary tuberculosis, or had produced meningitis.

5. *Cervical Gland Tuberculosis.*—Nine of these cases were investigated. In all the glands had been removed by operation. The cases were those typical of "strumous" glands in the neck, no other tuberculous lesion being discoverable.

6. *Cases of Primary Abdominal Tuberculosis.*—Nineteen of these cases were investigated. All occurred in children and showed some distinctive feature demonstrating the primary origin of the disease. In some there was ulceration of the intestine: in others tuberculous peritonitis. All showed caseation of the mesenteric glands. In some cases the patient died of generalised tuberculosis. In all cases the mesenteric glands were used for investigation, but in some of those in which there was generalisation of the disease lesions remote from the mesenteric glands were used, such as those occurring in the bronchial glands, lungs and the meninges.

7. *Joint and Bone Tuberculosis.*—Ten of these cases were investigated. They all occurred in adults with no other obvious tuberculous lesion, and comprised cases affecting the wrist (one case), elbow (one case), hip (one case), knee (four cases), ankle (two cases), spinal caries (one case). The material used for investigation was that removed by operation.

8. One case of tuberculosis of the *testicle* and one of the *kidney* were investigated. Both had been removed by operation.

9. One case of *lupus* was investigated.

The material which was obtained from the patients was used for investigation, either by making an emulsion of it, and injecting it into animals, or by injecting an emulsion into guinea-pigs and obtaining a culture from the lesions produced, or by both methods. In all cases a culture was obtained of each virus and used for investigation.

In the following table the viruses which have been completely investigated are grouped together as regards the virulence of the original virus on bovines and rabbits. The effects on these animals of the bacillus of bovine tuberculosis in certain doses have been found to be definite, so that the first comparison of the human virus and the bovine virus must be with regard to its effect on bovines and rabbits.

The classification is an artificial one and is based on the differences between the viruses investigated. The points of resemblance between the viruses are discussed on pages 80, 88 and 97.

TABULAR SUMMARY OF RESULTS.

Nature of Case	Part used for Experiment.	Viruses Virulent for Bovines and Rabbits.	Viruses Slightly Virulent for Bovines and Rabbits.	Viruses of irregular Virulence for Bovines and Rabbits.	Viruses Slightly Virulent at first for Bovines and Rabbits; becoming Virulent afterwards.
I.—Sputum. (4 cases.)	Sputum	H. 2, "Sp. A."	H. 1, "C.M." H. 62, "W.M."	—	H. 17, "Br. Sp. B."
II. — Primary Pulmonary Tuberculosis. (10 cases.)	Lung Lung, cervical gland.	—	H. 22, "F.W." H. 23, "J.P." H. 25, "A.T." H. 45, "F.M." H. 48, "W.P." H. 50, "P.H." H. 51, "H.M." H. 52, "T.F." H. 56, "F.T." H. 58, "F.G."	—	—
III. — General Tuberculosis. (1 case.)	Bronchial glands.	—	H. 35, "C.B."	—	—
IV. — Bronchial gland Tuberculosis. (4 cases.)	Bronchial glands.	—	H. 54, "C.W." H. 61, "E.C."	—	H. 13, "A.D." H. 21, "G.B."
V. — Cervical gland Tuberculosis. (9 cases.)	Cervical glands.	H. 28, "C.L." H. 29, "M.F." H. 31, "L.F."	H. 27, "B.D." H. 33, "R.T." H. 34, "C.U." H. 37, "O.J." H. 39, "M.B." H. 44, "D.C."	—	—
VI. — Primary abdominal tuberculosis. (19 cases.)	Mesenteric glands.	H. 7, "C.M." H. 10, "B.S." H. 14, "F.S." H. 19, "S.W." H. 20, "F.L." H. 38, "J.M."	H. 8, "S.C." H. 12, "H.N." H. 18, "T.T." H. 30, "E.M." H. 36, "M.D." H. 55, "R.D." H. 57, "B.J." H. 63, "G.R."	H. 49, "T.C."	
	Mesenteric gland, cervical gland, meninges.	—			
	Mesenteric gland, bronchial gland.	H. 32, "Y.W."			
	Mesenteric gland. lung, cervical gland, meninges.	H. 59, "L.B."			
	Mesenteric gland, meninges.	H. 64, "M.G."			
	Mesenteric gland, lung, meninges.	H. 65, "K.B."			
VII. — Joint Tuberculosis. (10 cases.)	Scrapings from joints. Pus from lumbar abscess.	—	H. 9, "C.T." H. 11, "E.D." H. 15, "I.W." H. 41, "A.S." H. 42, "M.R." H. 43, "F.F." H. 46, "H.W." H. 47, "S.B." H. 66, "W.C."	—	H. 16, "J.H."
VIII. — Tuberculosis of testicle.	Testicle	—	H. 40, "J.G."		
Of kidney. (2 cases.)	Kidney	—	H. 26, "E.M."		
IX.—Lupus. (1 case.)	Scrapings of the lesions.	—	—	H. 53, "D.H."	

In addition to these, in the early part of the work, an emulsion of a chronic tuberculous lung (H. 4, "M.L.") (dose of bacilli not estimated) was injected subcutaneously into two adult Jersey heifers. One animal was found normal at the end of 207 days. The other in 79 days showed a local tuberculous abscess and calcareo-caseous tubercle in the nearest glands. An emulsion of these lesions, injected into two normal heifers subcutaneously, and into one cow into the mamma, produced no result, all the animals, when killed in from 173 to 247 days, being found healthy.

In another case 10 cc. of sputum (H. 3) were injected into each of two places in a Jersey heifer. Only local lesions were found in 207 days.

H. 6 "U.H.," a case of abdominal tuberculosis, was used for injection into 3 adult bovines: minimal results followed. A monkey injected developed general tuberculosis. No cultures were investigated.

These three experiments are not included in the Table, as they can only be considered a very incomplete test of the virulence of a particular virus.

H. 24 "A.B." is excluded from the table as no tuberculosis was produced in guinea-pigs by it. H. 60 "W.B." is excluded, as some doubt existed as to the accuracy of the first experiments. H. 5 was not an experiment with an original human virus.

The experiments which have been performed with the viruses mentioned in the Table are as follows:—

1. Experiments in bovines by inoculation and feeding; in some cases with emulsions, in all with cultures.
2. Experiments in rabbits by inoculation and feeding.
3. Experiments in other animals, pigs, goats, monkeys, cats, dogs, rats, and the chimpanzee.

The results of the experiments will be considered according to the division made in the Table.

VIRUSES VIRULENT FOR BOVINES AND RABBITS.

The viruses included in this group are:—

H. 2, Sp. A., *sputum feeding;* H. 28 "C.L.," H. 29 "M.F.," H. 31 "L.F.," *cervical gland tuberculosis;* H. 7 "C.M.," H. 10 "B.S.," H. 14 "F.S.," H. 19 "S.W.," H. 20, "F.L.," H. 32 "Y.W.," H. 38 "J.M.," H. 59 "L.B.," H. 64 "M.G.," H. 65 "K.B.," *abandoned tuberculosis.*

Character of the Cultures.

In his investigation of the cultures of these fourteen virulent strains, Dr. Eastwood places them all in the three grades, which have already been described as comprising the viruses of bovine origin. (Bacillus of Bovine Tuberculosis, page 1.)

Grade I.—Contains H. 10 "B.S.," H. 14 "F.S.," and H. 28 "C.L.," H. 59 "L.B.," H. 64 "M.S.," H. 65 "K.B."

Grade II. contains H. 20 "F.L.," H. 29 "M.F.," H. 31 "L.F.," and H. 49 "T.C."

Grade III. contains H. 2, "Sp. A.," H. 7, "C. M.," H. 19, "S. W.," H. 32, "Y. W.," H. 38, "J. M."

(A) Effect of Inoculation and Feeding in Bovines.

1. *Inoculation into Bovines.*

Inoculation of Emulsions.

Ten out of the fourteen viruses were tested in this way; the exceptions were tested only in culture. **Emulsions.**

The emulsions were injected into calves and into adult bovines subcutaneously. A few were also injected intravenously, intraperitoneally and intramammarily. **Bovines.**

SUBCUTANEOUS INJECTION OF EMULSIONS INTO BOVINES.

Dose of T.B.	Number of Calves.	Result.*		Number of Adult Bovines.	Result.	
		G.T.	A.B.C.D.		G.T.	A.B.C.D.
5,000 to 12,000 - - -	4	3	C.	—	—	—
48,000 to 301,000 -	6	6	—	—	—	—
1 million to 5·09 million -	12	9	B. C. D.	5	4	D.
10 million to 15·8 million	3	3	—	—	—	—
355·5 million to 654·1 million -	5	5	—	4	4	—
901·4 million to 3.447 million -	7	7	—	3	3	—
And 9,132·8 million - - -						
Total - - -	37	33	4	12	11	1

* For explanation of the letters *see* p. 2.

If considered according to viruses, all these produced in one or other dose a generalised disease. The smallest dose which produced generalised tuberculosis was 5,000 tubercle bacilli (H. 10, "B. S."). A similar dose, however, of this virus produced only C. H. 49, "S.W." with 1·5 million tubercle bacilli, produced in one case acute tuberculosis, in another case C. This virus in an adult bovine, with 1·1 million, also produced D. With 53·4 million it produced in an adult bovine G.T. on two occasions. On the whole, judging from the emulsions, H. 19, "S.W." would not appear to be so virulent as some of the other strains. Although in large doses of culture it was very virulent to both calves and rabbits. H. 29, "M.F." is perhaps in the same category.

Of the calves fifteen out of the thirty-seven either died or were killed when dying. The remaining calves were killed at various periods when well, the longest period being 172 days. The shortest periods were as follows:—A calf died in 27 days from a dose of 3,447,000,000 tubercle bacilli (H. 20, "F.L."); another in 25 days (H. 28, "C.L.") of 901,000,000; another in 23 days (H. 14, "F.S.") of 362,000,000; another in 22 days (H. 32, "Y.W.") of 2,348,000,000 tubercle bacilli.

Of the twelve adult animals three died or were killed very ill. Two of the others were ill when killed, and the others were well when killed. The duration of life was between 21 days, with the largest dose (a bull that died), and 182 days, an animal that received 534,000,000 (H. 19, "S.W.").

Comparing these results with those obtained with the emulsions of viruses of bovine origin, the general correspondence of the results is to be noted; though the dose in different cases varied considerably, both in calves and in adult bovines, the great majority of the animals developed a generalised disease, which in many cases ended fatally.

(B) *Intramammary Inoculations.* Three stains were inoculated into each of two quarters of the mamma in three cows:—

994,000 tubercle bacilli (H. 10, "B.S.") inoculated into each of two quarters (Cow 295) produced only a local and minimal tuberculosis, although a generalised disease was produced in all the other bovines that were inoculated subcutaneously with the strain, except one (Calf 335).

Nineteen million tubercle bacilli (H. 14, "F.S.") into each of two quarters (Cow 75) produced acute tuberculosis of the mamma, and of the lymphatic glands as far as the iliac glands. The cow was very ill when killed in 34 days.

Twenty million tubercle bacilli (H. 28, "C.L.") injected into each of two quarters (Cow 143) produced acute tuberculosis of the mamma, and of the lymphatic glands as far as the iliac glands. The animal was killed when dying in 38 days.

Although only three experiments were performed, they are quite sufficient in number to show the similarity of the action of these virulent strains of human origin with the bovine strains in experimental tuberculosis of the udder.

(C) *Intravenous Inoculations.*—Only two strains were used (H. 2, "Sp. A." and H. 7, "C.M."). Two animals were injected with the former with 301,000 tubercle bacilli; two with the latter, 48,000 tubercle bacilli. All the animals died within 33 to 41 days from general tuberculosis.

(D) *Intraperitoneal Inoculations.*—The same two strains were used for intraperitoneal inoculations into four calves:—

602,000 tubercle bacilli (H. 2, "Sp. A.") killed a calf in 73 days with general tuberculosis.

48,000 tubercle bacilli (H. 7, "C.M.") killed a calf in 40 days with general tuberculosis.

301,000 tubercle bacilli (H. 2, "Sp.A.") and 48,000 tubercle bacilli (H. 7, "C.M.") were injected intraperitoneally, but the injection was found to be not into the peritoneum, but into the muscular subperitoneal tissues. Both remained well, and when killed showed a moderate degree of tuberculosis.

2. *Inoculation of Cultures into Bovines.*

All the viruses, fourteen in all, were tested as regards their virulence by subcutaneous injection of cultures into bovines. The total age of the cultures varied from five weeks to three years; the age of the individual culture used for inoculation was about three weeks. Cultures were injected subcutaneously in varying doses, two calves as a rule being used for each virus.

Inoculation of Culture in 50 Milligramme Doses.—With each strain two calves, as a rule, were inoculated, sometimes more. In all thirty-two calves were inoculated with 50 milligrammes. All except three died or were killed when dying in periods varying from 21 days to 81 days.

Of the two receptions one was killed well in 90 days (H. 10, "B.S."); the other was killed well in 90 days (H. 7, "C.M.").

All the calves showed generalised tuberculosis.

The disease produced by this large dose of culture was, as a rule, extremely acute and generalised, and is exactly comparable in its average duration, its appearances, anatomical distribution and microscopic structure to the acute disease caused by the injection of large doses of cultures of bovine origin.

Subcutaneous Injection of 43 *Milligrammes* (H. 28, "C. L."), of 30 *Milligrammes* (H. 31, "L. F."), and of 23 *Milligrammes* (H. 38, "J. M.") killed the calves with general tuberculosis.

10 *Milligramme Doses.*—Twelve of the viruses were each injected into two calves in doses of 10 milligrammes. The viruses which were not injected were H. 64, "M. G.," H. 65, "K.B." In some cases more than two calves were used. The object of injecting 10 milligramme doses was to compare with the similar experiments performed with the bovine viruses, and to see whether there was any variation in the virulence of the individual viruses when doses smaller than 50 milligrammes were given.

Thirty-two calves in all were inoculated. Twenty-five died or were killed when dying in from 19 to 69 days. They all showed general tuberculosis. The other calves were killed apparently well, in 90 days, and of these only three showed slight tuberculosis. The others showed a generalised tuberculosis, though not of an acute type. Those that showed slight tuberculosis were as follows:—

With Virus H. 28, "C. L." six calves were inoculated subcutaneously, each with 10 milligrammes. Five showed generalised tuberculosis, and one showed only slight tuberculosis (D.).

With Virus H. 59, "L. B." five calves were inoculated. Four died of acute tuberculosis one showed only slight tuberculosis (D.).

Of the two calves inoculated with Virus H. 20, "F.L." one died of acute tuberculosis, and the other showed slight tuberculosis (D.).

It cannot be said that these experiments bring out any variation in virulence of these viruses, and the small amount of disease obtained in a few of the instances can probably be explained as individual resistance on the part of the animal. A similar result was obtained with the bovine viruses when 10 milligrammes were used for inoculation (see page 58).

3. Feeding with Strains of Virulent Viruses.

Feeding Experiments. Calves.

Virus H. 7, "C.M."—One calf sucked Cow 73, in which very chronic and slight tuberculosis of the udder was produced by intramammary injection into two quarters of Virus H. 7, "C.M." The calf sucked for 170 days, and when killed showed calcareous foci in three mesenteric glands and no other lesion.

Virus H. 14, *"F.S."*—Another calf (181) sucked its mother (Cow 75) which had acute tuberculosis of the udder induced by injecting 19,000,000 tubercle bacilli (H. 14, "F.S.") into each of two quarters. The cow was killed when very ill in 34 days, and the sucking calf, killed in 114 days, showed numerous tuberculosis lesions in the intestine, caseation of all the mesenteric glands, and sparsely scattered tubercles in the liver, spleen, lungs, omentum, cervical and thoracic glands.

These are the only two experiments in sucking calves with virulent strains.

Another calf was fed with an emulsion of the prescapular gland and local lesion produced by an emulsion of a lesion of H. 2, "Sp. A." The lesion used, which was produced by a subcutaneous inoculation, was very slight and caseo-calcareous. The calf which was fed with this emulsion was killed in 69 days, and showed only a minimal lesion, namely, tuberculous nodules in two mesenteric glands.

Effects of Inoculation and Feeding in Rabbits and Guinea-pigs.

Inoculation. Rabbits.

The virulence of each of the viruses was tested in rabbits by means of the inoculation of both emulsions and cultures.

Injections of Emulsions into Rabbits.

Emulsions.

Ten of the viruses were injected in the form of emulsions into rabbits, and the following table shows the results:—

EMULSION INJECTIONS INTO RABBITS.

Virus.	Number of rabbits.	Intraperitoneal.	Intravenous.	Subcutaneous.	Number of cases of slight tuberculosis.	Dose of tubercle bacilli.
Cervical Glands.						
H. 29, "M.F." - - -	2	1 G.T.	1 G.T.	—	—	302 million. 151 „
H. 28, "C.L." - - -	4	2 „	2 „	—	—	19 million. (2.) 90 million. 225 „
H. 31, "L.F." -	2	1 „	—	1 G.T.	—	1·9 „
Abdominal Tuberculosis.						
H. 10, "B.S." - -	2	1 „	—	1 „	—	361,000.
H. 14. "F.S." - -	4	1 „	—	2 „	1. Intraperitoneal injection. (?) Subcutaneous and into cæcum.	Not estimated.
H. 19, "S.W." - - -	4	2 „	1 G.T.	1 „	—	„ „
H. 20, "F.L." -	10	5 „	4 „	1 „	—	2 „ „ 168,900. 675,000. 1·2 million. (2.) 31·5 million. (2.) 114·9 million. 143·6 „
H. 32, "Y.W." - -	4	2 „	—	2 „	—	31 million. (3.) 2 not estimated.
H. 49, "T.C." (mesenteric gland).	1	1 „	—	—	—	Not estimated.
H. 59, "L.B." (lung) - -	1	1 „	—	—	—	„ „
	34		33 G.T.		1	—

G.T. = General tuberculosis.

CULTURES.

The following Table shows the result of the Injection of Cultures into Rabbits.

CULTURE INJECTIONS INTO RABBITS.

Virus.	Number of Rabbits.	Duration of life in days.	Dose.	G. T.	S. T. or psorospermosis.	Died soon after injection.
Sputum—						
H. 2, "Sp.A." - -	4 5 4	17 to 42	10 mg. 1 mg. 0·1 mg.	13	—	—
Cervical Glands—						
H. 28, "C.L." - -	2 3 2 1	16 to 40	10 mg. 1 mg. 0·1 mg. 0·01 mg.	7	—	1
H. 29, "M.F." - -	2 3 3 3	11 to 91	10 mg. 1 mg. 0·1 mg. 0·01 mg.	10	1 Psorospermosis.	—
H. 31, "L.F." - -	2 2 2	25 to 108	10 mg. 1 mg. 0·1 mg.	5 —	— 1 chronic tubercle.	—
Abdominal Tuberculosis—						
H. 7, "C.M." - -	2 2 2 1	16 to 94	10 mg. 1 mg. 0·1 mg. 0·01 mg.	6 —	— 1 chronic tubercle.	—
H. 10, "B.S." - -	1 3 1 1	12 to 78	10 mg. 1 mg. 0·1 mg. 0·01 mg.	6	—	—
H. 14, "F.S." - -	2 5 6 1	14 to 94	10 mg. 1 mg. 0·1 mg. 0·01 mg.	13	—	1
H. 17, "S.W." - -	2 3 2 1	19 to 42	10 mg. 1 mg. 0·1 mg. 0·01 mg.	7	—	1
H. 20, "F.L." - -	2 3 2	17 to 30	10 mg. 1 mg. 0·1 mg.	7	—	—
H. 32, "Y.W." (Mesenteric Glands.)	1 1	21 to 30	1 mg. 0·1 mg.	2	—	—
H. 32, "Y.W." - (Bronchial Glands.)	1 1 1 1	12 to 32	10 mg. 1 mg. 0·1 mg. 0·01 mg.	4	—	—
H. 38, "J.M." - -	1 2 2 1 1	10 to 23	50 mg. 10 mg. 1 mg. 0·1 mg. 0·01 mg.	7	—	—
H. 59, "L.B." - -	4 4	18 to 70	1 mg. 0·1 mg.	5	—	3
TOTAL - -	101	—	—	92	3	6

Injections of all these viruses into rabbits, whether in the form of emulsions or of cultures produced in the majority of cases a generalised and usually acute disease, ending fatally. One case of severe chronic tuberculosis occurred with each of the Viruses H. 31, "L.F.," and H. 7, "C.M."

Feeding Experiments with Rabbits.

Two Rabbits fed with 10 milligrammes each of culture of H. 59, "L.B." in 51 and 74 days were found to have general tuberculosis. Two fed with 1 milligramme of the same virus showed in one case generalised tuberculosis in 90 days and in the other a slighter form of the disease, the animal dying in 37 days of biliary cirrhosis. Two rabbits fed with 10 milligrammes of culture H. 64, "M.G." showed: one, in 53 days general tuberculosis, the other in 91 days, a generalised disease not severe. Two fed with 1 milligramme showed slight generalised disease.

Culture Inoculations into Guinea-pigs.

Culture Inoculations. Guinea-pigs.

Guinea-pigs were inoculated intraperitoneally with doses of culture of 1 milligramme and 0·1 milligramme, four animals being used with the following viruses:—H. 2, "Sp. A."; H. 28, "C.L."; H. 29, "M.F."; H. 38, "J.M."; H. 14, "F.S."; H. 19, "S.W."; H. 20, "F.L."; H. 32, "Y.W." All the animals developed general tuberculosis. The other viruses in this group were also at one or other time tested on guinea-pigs, and produced general tuberculosis.

Feeding Experiments with Guinea-pigs.

Feeding Guinea-pigs.

Sixteen animals were fed with the milk of Cow 295 which had been inoculated with H. 10, "B.S." Three developed general tuberculosis, one slight tuberculosis, and the remainder were normal. Three guinea-pigs were fed with 1 milligramme of culture H. 64 "M.G." and 3 with 0·1 milligramme; five showed general tuberculosis, and one slight tuberculosis. Three guinea-pigs were fed with 1 milligramme of culture H. 59 "L.B." and 3 with 0·1 milligramme. All showed generalised tuberculosis, severe in three, and slight in three.

Experiments in Pigs.

Pigs.

Inoculation.—Four pigs were inoculated subcutaneously with culture H. 59, "L.B." Two inoculated respectively with 50 and 10 milligrammes died of severe general tuberculosis. Two that received 1 and 0·1 milligramme were killed in 84 and 86 days and showed generalized tuberculosis.

Feeding.—Two young pigs were fed for over 120 days with the milk of Cow 295 (Virus H. 10, "B.S."). They were killed in 129 and 121 days, and both showed caseation of the mesenteric glands. One showed no other lesion, but the other showed tubercles in the liver, the hepatic and bronchial glands, and one lumbar gland.

These pigs were fed with culture of H. 59, "L.B.," in doses of 10, 1, 0·1 milligrammes. They were all killed in about 90 days. The one that received the largest dose showed general tuberculosis, while the others showed a generalized disease of a milder type.

Experiments in Goats.

(A) *Inoculation Experiments* (*all subcutaneous*).

Goats.

Inoculation.

Virus H. 10, "*B.S.*"—A goat was inoculated with an emulsion from a lesion of a previously inoculated calf (113), dose 1,800,000 tubercle bacilli. It died of general tuberculosis.

A second goat received a dose of culture from the same calf, 1,800,000 tubercle bacilli. It was killed in 198 days, and showed disseminated tuberculosis.

Virus H. 14, "*F.S.*"—A goat received 4,500,000 tubercle bacilli, of emulsion of a lesion from an inoculated heifer (197). It died in 75 days of general tuberculosis.

Virus H. 28, "*C.L.*"—A goat received 5,000,000 tubercle bacilli in an emulsion from previously infected calf (515). It died in 96 days from generalised tuberculosis.

Virus H. 32, "*Y. W.*"—A goat received 155,000,000 tubercle bacilli in an emulsion of a tuberculous gland from a calf infected with Virus H. 32, "Y.W." It was killed in 27 days when very ill, and showed general miliary tuberculosis.

Virus H. 19, "*S.W.*"—A goat received 53,000,000 tubercle bacilli in an emulsion of a tuberculous lesion from Calf 271, infected with Virus H. 19, "S.W." It was killed when dying in 77 days, and showed general tuberculosis.

(B) *Feeding Experiments.*

Virus H. 31, "*L.F.*"—Two goats were fed each with 10 milligrammes of culture derived direct from human cervical glands. They both showed severe tuberculosis of the intestines and mesenteric glands, and general dissemination of the disease. One died in 199 days, the other was killed when dying in 106 days after feeding. Feeding.

EXPERIMENTS WITH MONKEYS.

(A) *Inoculation Experiments.*

Virus H. 7, "*C.M.*"—A monkey received subcutaneously a small dose (tubercle bacilli not estimated) of the emulsion of the mesenteric glands of the patient from whom the specimen was obtained. It died in 69 days with general tuberculosis. Monkeys. Inoculation.

(B) *Feeding Experiments.*

Virus H. 10, "*B.S.*"—A baby monkey was fed with the tuberculous milk of Cow 295 for 128 days. When killed it showed no tuberculosis. Cow 295 had developed very slight disease of the udder. Feeding.

Four monkeys were fed each with a single dose of culture of Virus H. 10, "B.S." The doses used were 0·01, 0·1, 1, and 10 milligrammes. The one that received the smallest dose was killed after 2½ years and showed general tuberculosis. There was no disease of the intestines; the lungs were most severely affected. The other three died, or were killed when very ill, in 79, 99 and 151 days. They all showed general tuberculosis with disease of the intestine and mesenteric glands.

Virus H. 28, "*C.L.*"—Two baby monkeys received one dose each of 90 cc. of milk containing 5,000,000 tubercle bacilli. They both died in 80 and 88 days respectively, and showed general tuberculosis.

EXPERIMENTS IN CHIMPANZEES.

Inoculation.—A chimpanzee received subcutaneously 1 mg. of culture, H. 59, "L.B." It died in 79 days of acute general tuberculosis. Chimpanzees.

Feeding.—No feeding experiments have been performed.

EXPERIMENTS IN CATS.

(A) *Inoculation Experiments.*

Cats.

No inoculation experiments have been performed. Inoculation.

(B) *Feeding Experiments.*

Virus H. 28, "*C.L.*"—Three cats were fed with the tuberculous milk of Cow 143. The milk contained numerous tubercle bacilli, containing about 35,000 tubercle bacilli per cubic centimetre. Feeding.

One cat received eighteen pints of milk. It died in 100 days from acute pleurisy (non-tuberculous), and showed caseation of the mesenteric and thoracic glands.

Another cat received about seven pints of milk in all. It died in 112 days of pneumonia, and showed some fibrous tubercles and numerous tubercle bacilli in the lungs.

The third cat was fed with about two pints of milk. It was killed in 93 days, and showed a tuberculous lesion in one ileo-colic, and one mesenteric gland, and numerous fibrous calcareous tubercles in the lungs.

EXPERIMENTS IN DOGS.

Inoculation.—A dog received intraperitoneally 10 milligrammes of culture, H. 59, "L.B." It died in 37 days and showed tuberculous peritonitis and general miliary tuberculosis. Dogs.

Feeding.—No feeding experiments have been performed.

EXPERIMENTS IN RATS AND MICE.

Rats and Mice.

(A) *Inoculation Experiments.*

Inoculation.

Six rats were inoculated with large doses of culture from H. 20, "F.L.," H. 28, "C.L.," H. 29, "M.F.," H. 49, "T.C.," and H. 16, "J.H." The individual doses given were 30 milligrammes, 50, 70, 75, and in two cases 100 milligrammes. The animals all died in periods of from 33 to 213 days and they showed only a few lesions, but very numerous tubercle bacilli in all the organs, a condition which has been called "tuberculous septicæmia." Rats.

(B) *Feeding Experiments.*

Rats Feeding.

Eleven rats were fed with tuberculous milk (H. 10 "B.S.") and the tuberculous organs of guinea-pigs from various sources for long periods, from 80 to 360 days. Only one of the rats showed any lesion, which consisted only of two or three small foci in the lung.

(A) *Inoculation Experiments.*

Mice.

Two mice each received subcutaneously 2,670,000 tubercle bacilli in an emulsion of a tuberculous lesion of Calf 271, inoculated with H. 19 "I.W.". In one mouse a few translucent tubercles were found in the lungs when killed in 35 days; in the other mouse which died in 14 days, a caseous focus was found near the seat of injection.

(B) *Feeding Experiments.*

Feeding.

Eight mice were fed in the same way as the rats, and with the same material. They lived from 40 to 224 days, and showed no tuberculosis on examination.

GENERAL RESULTS.

The human viruses which are discussed in this group resemble the bacillus of bovine tuberculosis in the following points:—

1. Their cultural characters are the same as those of the bacillus of bovine tuberculosis, and only one kind of bacillus was found.

Of the 14 human viruses in this group, 3 were obtained from tuberculous cervical glands, 10 from cases of abdominal tuberculosis, and one was obtained as the result of sputum feeding. In the cases of abdominal tuberculosis, in 3 cases (H. 32 "Y.W." H. 59 "L.B." and H. 64, "M.S.") not only the mesenteric glands but the remote lesions were tested, viz., those occurring in the lungs and meninges. The virulence of the bacillus and its characters were the same in all the lesions.

In the sputum feeding case, a virulent bacillus was obtained from the minimal lesions, resulting from prolonged feeding of a heifer cow with human sputum.

2. They produce an acute tuberculosis by subcutaneous injection into bovines, and to a less extent by feeding.

3. In rabbits they also produce a generalised tuberculosis by inoculation and feeding.

4. They are also virulent for pigs, goats, monkeys, and the chimpanzee. Dogs are susceptible by intraperitoneal inoculation.

5. They produce the same result as the bovine bacillus in rats by inoculation, namely, a wide distribution of the bacillus in the body, without the formation of visible lesions.

VIRUSES SLIGHTLY VIRULENT FOR BOVINES AND RABBITS.

These viruses are 40 in number, and are shown in Column II. in Table.

Characters of the Cultures Obtained.

Dr. Eastwood separates the cultures obtained from these slightly virulent viruses from those obtained from the virulent viruses and from those of bovine tuberculosis. These are all placed in Grades I., II., and III. Slightly virulent viruses he places in Grades IV. and V.

Grade IV. is characterised by the growth of the bacilli in broth being more vigorous than in Grade III., by a more rapid and wrinkled growth on glycerin-agar, and a heaped-up growth on potato with slight pigmentation.

In Grade V. the growth is luxuriant on all the three media, and on potato there is a richly pigmented growth.

Grade IV.—The following viruses come within this grade:—

H. 8, "S.C."
H. 9, "C.T."
H. 18, "T.T."
H. 30, "E.M."
H. 34, "C.U."
H. 35, "C.B."
H. 36, "M.D."
H. 39, "M.B."
H. 42, "M.R."
H. 50, "P.H."
H. 52, "T.F."
H. 55, "R.D."
H. 58, "F.G."
H. 61, "E.C."
H. 62, "W.M."
H. 63, "G.R."

Comprising 4 cases of pulmonary tuberculosis.
,, 1 ,, of "general" tuberculosis.
,, 1 ,, of bronchial gland tuberculosis.
,, 2 ,, of cervical gland tuberculosis.
,, 6 ,, of abdominal tuberculosis.
,, 2 ,, of joint tuberculosis.

Grade V.—In this grade come the following viruses:—

H. 11, "E.D."
H. 12, "H.N."
H. 15, "I.W."
H. 22, "F.W."
H. 23, "J.P."
H. 25, "A.T."
H. 26, "E.M."
H. 27, "B.D."
H. 33, "R.T."
H. 37, "O.J."
H. 40, "J.G."
H. 41, "A.S."
H. 43, "F.F."
H. 44, "D.C."
H. 45, "F.M."
H. 46, "H.W."
H. 47, "S.B."
H. 48, "W.P."
H. 51, "H.M."
H. 54, "C.W."
H. 56, "F.T."
H. 57, "B.J."

Comprising 7 cases of pulmonary tuberculosis.
,, 4 ,, of cervical gland tuberculosis.
,, 1 ,, of bronchial gland tuberculosis.
,, 2 ,, of abdominal tuberculosis.
,, 6 ,, of joint tuberculosis.
,, 1 ,, of kidney tuberculosis.
,, 1 ,, of testicle tuberculosis.

H. 1, "C.M."
H. 66, "W.C."
Not classified.

EFFECT OF THE INOCULATION OF SLIGHTLY VIRULENT VIRUSES IN BOVINES AND RABBITS.

With regard to the first virus, that of H. 1, "C.M.," the origin of this was a culture obtained from guinea-pigs which had been injected with sputum from a tuberculous patient; it was subcultured for five months before inoculation into bovines. The dose was in no case estimated, and the results therefore may be stated very shortly.

Two adult animals inoculated subcutaneously were normal throughout, they were killed in 170 and 174 days. Two other adult animals showed only a local lesion in over 100 days. Four cows received doses into each of two quarters of the udder. Two of these showed only slight induration of the udder when killed. Another was normal throughout, and the fourth (Cow 3) showed tuberculosis of the infected quarters of the udder, but no obvious tuberculosis in the neighbouring glands. A calf, which was sucking this cow, was killed in twenty-two days, and showed numerous caseo-calcareous nodules in the mesenteric glands, but no other disease.

Six monkeys subcutaneously inoculated with the culture died of general tuberculosis.

(A) *Into Bovines.*

Bovines.

The results with the remaining viruses are shown in the following Table, in which the effect of culture inoculations is placed side by side with that of the emulsions of tuberculous lesions. In the case of the cultures, into each calf 50 milligrammes were injected subcutaneously, and the result is shown according to the viruses.

TABLE SHOWING RESULTS OF CULTURE AND TISSUE EMULSION SUBCUTANEOUS INOCULATIONS WITH SLIGHTLY VIRULENT VIRUSES.

Virus.	Culture 30 mg.* in each Calf.	Emulsions in Calves.	
	Result.**	Dose of tubercle bacilli.	Result.
Sputum:			
H. 62, "W.M."	B. and D.		
General Tuberculosis:			
H. 35, "C.B."	B. and D.		
Pulmonary Tuberculosis:			
H. 22, "F.W."	D. and D.	242,000	B.
		3·2 million	C.
		14·2 million	B.
		100 million.	B.
H. 23, "J.P."	B. and D.	8·1 million	B.
		16 million	B.
		103 million (2 calves)	B. G.T slight.
H. 25, "A.T."	B. and B.	87 million	C.
		1,005 million	B.
H. 45, "F.M."	D., A. and B†		
H. 48, "W.P."	B. and B.		
H. 50, "P.H."	B. and D.		
H. 51, "H.M."	D. and D.		
H. 52, "T.F."	B. and D.‡		
H. 56, "F.T."	B. and B.§		
H. 58, "F.G."	D.		
Bronchial Glands:			
H. 54, "C.W."	B.		
H. 61, "E.C."	D.‖		
Cervical Glands:			
H. 27, "B.D."	D. D.	40·9 million (2 calves)	B. B.
H. 33, "R.T."	B. D.		
H. 34. "C.U."	B. B.		
H. 37, "O.J."	C. D.		
H. 39, "M.B."	B. B.		
H. 44, "D.C."	C. D.		
Mesenteric Glands:			
H. 8, "S.C."	D. D. B.¶ B.¶	6 million (2 calves)	B. B.
		12·5 million (2 calves)	C. C.
		809·8 million	B.
		5,124 million	B.
H. 12, "H.N."	C. B.	13,000 (3 calves)	B. D. D.
		310,000	B.
		2·7 million (2 calves)	B. C.
		103·9 million (2 calves).	B. D.
		3,140 million	C.

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* A note is made where the dose exceeded 50 milligrammes. † Dose of 275 milligrammes.
‡ Doses of 100 and 150 milligrammes. § Dose of 100 milligrammes. ‖ Dose of 183 milligrammes.
¶ Doses of 3,000 milligrammes. ** For explanation of letters *see* page 2.

TABLE SHOWING RESULTS OF CULTURE AND TISSUE EMULSION SUBCUTANEOUS INOCULATIONS WITH SLIGHTLY VIRULENT VIRUSES—*continued.*

Virus.	Culture 50 mg. in each Calf.	Emulsions in Calves.	
	Result.	Dose of T.B.	Result.
Mesenteric Glands—cont.			
H. 18, "T.T."	B. D.	4·4 million (3 calves)	B. B. G.T. slight.
		269·9 million (2 calves)	B. G.T. slight.
		2,814 million	B.
H. 30, "E.M."	B. D.	4,756 million (2 calves)	C. D.
H. 36, "M.D."	B. D.	15·5 million (2 calves)	B. B.
H. 55, "R.L."	B. B.		
H. 57, "B.J."	D.		
H. 63, "G.R."	B. B. B.*		
Joints :—			
H. 9, "C.T."	B. B. C.† G. T. very slight.†	9 million	
		133 million	D.
H. 11, "E.D."	B. D.	1 million	B.
		21·9 million	B.
		479 million	C.
H. 15, "I.W."	Not complete	3 million	B.
		3·7 million (2 calves)	C. D.
		14 million	A.
		68 million	D.
		136 million	C.
		261 million	B.
H. 41, "A.S."	B. B.	—	—
H. 42, "M.R."	B. B.	—	—
H. 43, "F.F."	B. B.	—	—
H. 46, "H.W."	C. D.	—	—
H. 47, "S.B."	B. D.		
H. 66, "W.C."	B. D.		
Testicle :—			
H. 40, "J.G."	B. B.	—	—
Kidney :—			
H. 26, "E.M."	C. D.		

* Dose of 100 milligrammes.

† Dose of 750 milligrammes.

All the animals inoculated with culture were killed in about ninety days except two, one of which died of pneumonia in eighty-three days, and the other died from an undetermined cause in sixty-one days.

The results of inoculation of the cultures show generally that with all these viruses the large doses given produced only a limited and not a progressive tuberculosis.

The results of the emulsion inoculations show the same point, with the exception of two viruses, H. 23 "J.P.," and H. 18 "T.T." These exceptions may now be considered.

H. 23 "J.P."—Of two animals inoculated subcutaneously with 103,000,000 bacilli of the Virus H. 23 "J.P.," one was killed in 79 days and showed only B, while the other showed slight illness, and was killed in 61 days. In this animal (Calf 365) there was a caseous local lesion and tuberculous nodules in the prescapular gland and in other lymphatic glands (the left gluteal, left submaxillary, and all the mesenteric). Many minute tubercles were present in the lungs and liver, only a few in the kidneys. This was therefore a case of spreading tuberculosis, the calf being perhaps more susceptible than its fellow inoculated at the same time with the same dose. Dr. Eastwood considered from the microscopic examination that the lesions were retrogressing.

H. 18, "*T.T.*"—In this virus two calves injected subcutaneously, when killed well, showed some generalisation of the disease. One calf (165) had received a dose of 4·4 million, and when killed in 57 days showed, besides the local lesion, a caseous and calcareous prescapular gland, fairly numerous minute tubercles in the lungs and thoracic glands, four small minute tubercles in the liver, and calcareous foci in one mesenteric gland. The other calf, inoculated with 269,000,000 bacilli, was killed in 65 days (Calf 405), and showed a local caseous lesion, casous nodules in the prescapular and prepectoral glands, and very numerous minute tubercles in the lungs.

Intravenous Inoculation—H. 22, "*F.W.*"—Two calves inoculated with this virus both showed disseminated lesions. Calf 399 received 709,000,000 of an emulsion of guinea-pig lesions. It showed tuberculous lobular pneumonia and tuberculosis of the thoracic glands, while there were tubercle bacilli in enormous numbers in all the principal organs and glands, even where no lesions were visible.

An emulsion of the thoracic glands of this calf, containing 20,000,000 tubercle bacilli, was injected intravenously into another calf (457). The calf died in 57 days, and showed acute miliary tuberculosis of the whole of both lungs with intense congestion, caseation of all the thoracic glands, and a few tuberculous foci in the intestine and mesenteric glands. Tubercle bacilli was found in those mesenteric glands which appeared to be healthy.

An emulsion of the bronchial glands of this calf was injected intravenously into another calf in a dose of 11,000,000 tubercle bacilli. It was killed in 62 days, and showed three small tubercles in the lungs and a few calcareous grains in the thoracic glands.

H. 8, "*S.C.*"—The calf which received 728,000,000 tubercle bacilli showed early general tuberculosis in the lungs and glands of the body, the tubercles in the thoracic glands being in an early stage of caseation.

The calf which received 41,000,000 intravenously showed very numerous tubercles in the lungs and many in the other principal organs. The thoracic glands were very large and caseous. Tubercles were also seen in the suprarenals, in many mesenteric glands in the precrural, prescapular, and right pharyngeal glands. Anatomically the lesions found were not unlike those produced in the H. 22, "F.W.," animal which received 20,000,000 tubercle bacilli.

H. 12, "*H.N.*"—The calf that received 103,000,000 intravenously showed very widely spread miliary tuberculosis of the lungs, liver, kidneys, suprarenals, and intestine. There were small caseous foci in nearly all the lymphatic glands, especially the mesenteric. The thoracic glands contained very numerous but caseous nodules.

Dr. Eastwood reports that as regards the histological changes which he has studied in one by these animals (H. 8, "S.C.," Calf 305) "the lesions resemble in type the lesions produced by large doses of virulent cultures, and differ only in degree. There is less fibrin formation and less tissue destruction."

Intraperitoneal.—Only one animal was inoculated intraperitoneally with an emulsion. A calf received 479,000,000 tubercle bacilli (H. 11, "E.D."). It was killed well in 160 days, and showed slight tuberculosis only.

INJECTIONS OF SLIGHTLY VIRULENT VIRUSES INTRAPERITONEALLY INTO RABBITS.

(The results are shown in the following Table, cultures and emulsions side by side.)

Virus.	Cultures.			Tissue emulsions.		
	Number of Rabbits.	Dose in mg.	Result.	Number of Rabbits.	Result.	Dose.
Sputum—						
H. 63, "W.M."	2	1· 1·	—	—	—	
Pulmonary Tuberculosis—						
H. 22, "F.W."	1	50·0	S.T.*	9	S.T.	213,000 (2) 1 to 2 million (2) 11 million (1) 20 „ (2) 54 „ (2)
H. 23, "J.P."	3	50·0 10·0 1·0	S.T.	2	S.T.	10 „ (2)
H. 25, "A.T."	6	50·0 10·0 10·0 10·0 1·0 1·0	S.T.	3	S.T.	4·5 „ 18 „
H. 45, "F.M."	3	50·0 10·0 1·0	S.T.	—	—	—
H. 48, "W.P."	4	50·0 10·0 1·0 0·1	S.T.	—	—	—
H. 50, "P.H."	4	50·0 10·0 1·0 0·1	Nil. T.P.† S.T. Nil.	—	—	—
H. 51, "H.M."	5	10·0 1·0 1·0 1·0 0·1	S.T.	—	—	—
H. 52, "T.F."	4	10·0 1·0	G.T.‡ Psor.§	—	—	—
		1·0 0·1	S.T.			
H. 56, "F.T."	4	10·0 1·0 1·0 0·1	S.T.	—	—	—
H. 58, "F.G."	4	10·0 1·0 1·0 1·0		—	—	—
General Tuberculosis.						
H. 35, "C.B."	3	50·0 10·0 1·0	S.T.	—	—	—
Cervical Glands.						
H. 27, "B.D."	4	50·0 10·0 1·0	S.T.	—	—	—

* Slight tuberculosis.
† Tuberculous peritonitis.
‡ Generalized tuberculosis.
§ Psorospermosis.

INJECTIONS OF SLIGHTLY VIRULENT VIRUSES INTRAPERITONEALLY INTO RABBITS—*continued.*

Virus.	Cultures.			Tissue emulsions.		
	Number of Rabbits.	Dose in mg.	Result.	Number of Rabbits.	Result.	Dose.
Cervical Glands—cont.						
H. 33, "R.T."	3	50·0	G.T.	—	—	—
H. 34, "C.U."	2	10·0 1·0	S.T.	—	—	—
H. 37, "O.J."	3	50·0 10·0 1·0	S.T.	—	—	—
H. 39, "M.B."	3	50·0 10·0 1·0	S.T.	—	—	—
H. 44, "D.C."	5	50·0 10·0 5·0 1·0 1·0	S.T.	—	—	—
Mesenteric Glands.						
H. 8, "S.C."	3	10·0 1·0 0·1	S.T.	6	5 S.T. 1 nil.	5 not estimated. 5 million (1).
H. 12, "H.N."	3	50·0 10·0 1·0	S.T.	4	2 nil. 2 S.T.	11 million. 157 „ and less.
H. 18, "T.T."	9	50·0 33·0 33·0 10·0 10·0 1·0 1·0 0·1 0·1	S.T.	6	1 nil. 5 S.T.	4 not estimated. 10·7 million (2).
H. 30, "E.M."	5	50·0	Acute T.P.	3	S.T.	1 not estimated. 158 million. 1,427 „
		10·0 10·0 1·0 1·0	S.T.			
H. 36, "M.D."	3	50·0 10·0 1·0	S.T.	—	—	—
H. 55, "R.D."	4	10·0 1·0 1·0 0·1	S.T.	—	—	—
H. 57, "B.J."	3	10·0 10·0 10·0	—	—	—	—
H. 63, "G.R."	6	10·0 1·0 1·0 1·0 1·0 1·0	S.T. T.P. T.P.	—	—	—
Joints—						
H. 9, "C.T."	5	50·0	G.T.	2	S.T.	456,000.
		50·0 10·0 10·0 1·0	S.T.	—	—	—
H. 11, "E.D."	5	50·0	T.P. died.	2	S.T.	1 not estimated. 1 million.
		50·0 10·0 10·0 1·0	S.T.	—	—	—

INJECTIONS OF SLIGHTLY VIRULENT VIRUSES INTRAPERITONEALLY INTO RABBITS—*continued.*

Virus.	Cultures.			Tissue Emulsions.		
	Number of Rabbits.	Dose in mg.	Result.	Number of Rabbits.	Result.	Dose.
Joints—cont.						
H. 15, "I.W."	—	—	—	6	S.T.	1 not estimated. 4 million (2). 8 „ (1). 29 „ (2).
H. 41, "A.S."	3	50·0 10·0 1·0	S.T.	—	—	—
H. 42, "M.R."	3	50·0 10·0 1·0	S.T.	—	—	—
H. 43, "F.F."	5	50·0	G.T.	—	—	—
		50·0 10·0 1·0	S.T.	—	—	—
H. 46, "H.W."	3	50·0 10·0 1·0	S.T.	—	—	—
H. 47, "S.B."	3	50·0 10·0 1·0	S.T.	—	—	—
Testicle—						
H. 40, "J.G."	3	50·0 10·0 1·0	S.T.	—	—	—
Kidney—						
H. 26, "K.M."	—	Not injected.				

It will be noted that in the majority of cases, culture inoculation, whatever dose was given, produces only a slight degree of tuberculosis, but in a certain number of cases general tuberculosis resulted, and caused the death of the animal. These viruses are:—*pulmonary tuberculosis*, H. 50, "P.H."; H. 52, "T.F." *Cervical glands*, H. 33, "R.T." *Abdominal tuberculosis*, H. 30, "E.M." *Joints*, H. 9, "C.T."; H. 11, "E.D."; H. 43, "F.F." The anatomical lesions produced in these cases were those of tuberculosis. These viruses only occasionally produced a generalised disease in the rabbits. In the other inoculations done with the viruses, the disease produced was for the most part minimal. Only one of these viruses, viz., H. 9 "C.T.," produced some generalisation of disease in the calf, and that with a very large dose, 750 milligrammes.

EXPERIMENTS WITH PIGS.

(A) *Inoculation Experiments.*

Virus H. 56, "F.T." (*Pulmonary Tuberculosis*).—One pig received fifty milligrammes of culture subcutaneously. Killed in 65 days, it showed a very slight local lesion with a caseous gland. There were numerous translucent tubercles in the lungs, containing tubercle bacilli. A second pig, receiving fifty grammes subcutaneously, showed in 91 days, slight tuberculosis: locally, in the neighbouring gland and in the lungs.

Another pig, receiving one milligramme subcutaneously, was killed in 98 days, and showed a small caseous local lesion, one caseous area in a neighbouring gland, and a number of small caseous tubercles in the lungs and very few in the liver, spleen, and mesenteric glands.

Virus H. 50, "P.H." (*Pulmonary Tuberculosis*).—Two pigs each received fifty milligrammes of culture subcutaneously. Slight tuberculosis only resulted.

(B) *Feeding Experiments.*

Virus H. 56, "F.T." (*Pulmonary Tuberculosis*).—One pig was fed with fifty milligrammes of culture. Killed in 98 days, it showed no lesion in the intestine but large caseous foci were present in the submaxillary and mesenteric lymphatic glands. There was no other tuberculous lesion.

Another pig fed with fifty milligrammes showed in 91 days slight tuberculosis.

One pig fed with one milligramme of culture was killed in 99 days, and showed caseous foci in the submaxillary and neighbouring lymph glands, a few foci in the mesenteric glands. There were three fibrous foci in the lungs (no tubercle bacilli found).

Virus H. 50, "P.H." (*Pulmonary Tuberculosis*).—Two pigs were fed, each with fifty milligrammes. One killed in 93 days showed one nodule in the lung. The other, killed in 92 days, showed no tuberculosis.

General Results.—The experiments with pigs are still being continued. Those received showed that the pig is but little affected by this group of viruses.

Dogs.

EXPERIMENTS WITH DOGS.

Inoculation.

(A) *Inoculation Experiments.*

Virus H. 8, "S.C." (*Abdominal Tuberculosis*).—Two dogs inoculated subcutaneously with 1 milligramme of culture were killed in about 90 days and showed only a few nodules in the internal organs.

Virus H. 63, "G.R." (*Abdominal Tuberculosis*).—Two puppies each received 10 milligrammes of culture intraperitoneally. In one killed 85 days after injection was found to be partly intramuscular; very slight tuberculosis was found. The other died in 48 days of acute tuberculous peritonitis and general tuberculosis.

(B) *Feeding Experiments.*

Feeding.

Virus H. 8, "S.C."—Two dogs were fed; one with 10 milligrammes, the other with 1 milligramme; killed in 100 days, only traces of disease were found in the internal organs.

Virus H. 25, "A.T." (*Pulmonary Tuberculosis*).—Two dogs were fed with 10 milligrammes and 1 milligramme. One (with 10 milligrammes) died in 94 days showing slight disease of mesenteric glands, tuberculosis of lung, pneumo-thorax and empyema. The other (1 milligramme) killed in 191 days showed sparsely scattered tubercles in the internal organs.

General Results.—The results are closely similar to those obtained with the bovine virus (*see* p. 12).

EXPERIMENTS ON MONKEYS.

(A) *Inoculation.*

Monkeys.
Inoculation.

Virus H. I, "C.M." (*Sputum*).—Six monkeys were inoculated subcutaneously with an emulsion of diseased organs from animals inoculated with Virus H. I, "C.M." The dose of tubercle bacilli was not estimated. All the animals died of general tuberculosis.

Virus H. 6, "U.H." (*Pulmonary Tuberculosis*). A monkey inoculated subcutaneously with an emulsion of a human tuberculous lung died of general tuberculosis in 37 days.

Virus H. 8, "*S.C.*" (*Abdominal Tuberculosis*).—A monkey inoculated subcutaneously with an emulsion of the mesenteric glands of the patient, died in 68 days of general tuberculosis.

Virus H. 61, "E.C." (*Bronchial Gland Tuberculosis*).—One monkey received 0·1 milligramme of culture subcutaneously, and another 0·01 milligramme subcutaneously. They died in 84 and 89 days, both of general tuberculosis.

(B) *Feeding Experiments.*

Feeding.

Virus H. 56, "F.T." (*Pulmonary Tuberculosis*).—A baboon fed with one milligramme of culture was killed when dying in 108 days, and showed general tuberculosis.

EXPERIMENTS IN CHIMPANZEES.

Chimpanzees.

Virus H. 25, "A.T." (*Pulmonary Tuberculosis*).—A chimpanzee received one milligramme of culture subcutaneously. It died in 50 days of acute miliary tuberculosis.

Another chimpanzee was fed with one milligramme of culture, and died in 77 days of general tuberculosis.

GENERAL RESULTS.

The human viruses discussed in this group have the following characteristics:—

1. They differ somewhat in cultural characters from the viruses of bovine tuberculosis and the human viruses virulent for bovines and rabbits, being generally more luxuriant in growth, and becoming pigmented when grown on potato.

2. When inoculated into calves, even in large doses, they will not produce the generalised disease that the bovine bacillus produces. In some cases only local disease is produced; in others the disease extends to the nearest of the lymphatic glands; and in a few others scattered tubercles were found in the lungs and a few internal glands of the body. From subcutaneous inoculation, however, no death has resulted.

3. In rabbits only a local disease is produced in the majority of instances. In a few cases, however, an acute form of a generalised disease is produced.

4. The viruses slightly virulent for bovines and rabbits produce an acute tuberculosis and death of the animal, both by feeding and inoculation, in monkeys and in the chimpanzee.

5. The disease microscopically in monkeys and the chimpanzee is the same as that produced by the viruses virulent to calves and rabbits. In some cases the lesions first produced in rabbits and calves are like those produced by virulent viruses, although the lesions are retrogressive and not progressive.

6. The experiments with pigs are incomplete. In dogs these viruses behave like the bovine viruses.

VIRUSES OF IRREGULAR VIRULENCE FOR BOVINES AND RABBITS.

(Column III. in Table.)

Two viruses of those investigated come under this class. H. 53, "D.H.," was a case of lupus in a child, and the scrapings of the lesion were used for investigation.

H. 49, "*T.C.*" Was a case of primary abdominal tuberculosis in a child in which the mesenteric glands were enlarged and of stony hardness. The lungs contained numerous hard grey fibrous tubercles and there were a few tubercles in the bronchial glands. The mesenteric gland lesion was very old; that of the lung being more recent. The mesenteric glands and lung were used for investigation, but the experiments with the lung failed, the guinea-pigs dying of an accidental injection.

The results obtained in these cases will be considered individually.

Bovines. Inoculation.

Virus H. 53, "*D.H.*" (*Lupus*)—Three calves received subcutaneously each 50 milligrammes of a culture of the original material obtained through a guinea-pig. The calves were killed well in 90 and 91 days. Two calves showed slight tuberculosis (D), and one showed a more generalised tuberculosis, which, however, did not kill the animal within 90 days.

From one of these calves (905) a culture was obtained, and when injected into two calves in a dose of 50 milligrammes produced in one only a minimal tuberculosis (B) in 103 days, and in the other a more generalised disease in 88 days. Both animals were killed when quite well.

Two calves were inoculated each with doses of 10 milligrammes of culture obtained from one of the calves (905). They were both killed when well in 88 days. One showed a moderate degree of generalised tuberculosis; the other showed slight tuberculosis (D).

These results are very different from those obtained by inoculation, either with the bacillus of bovine tuberculosis or with the virulent viruses obtained from cases of human tuberculosis: they show a degree of virulence higher than that of the viruses in Column II. of Table.

Rabbits. Inoculation.

Ten animals were injected intraperitoneally in doses of 10 milligrammes (two), 1 milligramme (four), 0·1 milligramme (three), 0·01 milligramme (one). They all died in from 14 to 74 days with acute general tuberculosis. In this respect, therefore, the virus H. 53, "D.H.," agrees with the bovine virus and with the virulent viruses of human origin.

Bovines. Inoculation.

Virus H. 49, "*T.C.*" (*Abdominal Tuberculosis*).—With this virus two calves were inoculated subcutaneously with 50 milligrammes of culture of original material, two months old. One died in 81 days of acute generalised tuberculosis; one was killed well in 83 days, and showed only slight tuberculosis. A culture obtained from the latter calf was injected into two calves in a dose of 50 milligrammes. Both calves died of acute generalised tuberculosis in 21 and 39 days. This same culture produced death in two calves from general tuberculosis when given in 10 milligramme doses. The culture of the original material in 10 milligramme doses produced a slighter effect than this, only one calf dying. There was therefore some increase of virulence after passing the virus through one calf. Although the culture of the original material when 7 months old produced generalised tuberculosis in two calves, when it had been grown for 14 months it was found to be much less virulent when injected into one calf (1,097) in a dose of 50 milligrammes. The culture had apparently lost virulence by subculture.

Rabbits. Inoculation.

The results obtained with the cultures in rabbits show the same irregularity as those obtained with the calves.

Cultures of the *original material* of different ages were inoculated as follows:—

1. *Culture Two Months old.*—Four rabbits, in doses of 50, 10, 1 and 0·1 milligrammes. All died, but while the disease was severe in three of the animals it was only slight in the one injected with 50 milligrammes. The amount of disease in the last animal was about the same as that observed when the slightly virulent human viruses are injected into rabbits.

2. *Culture Seven Months old.*—In four rabbits; doses of 10, 1, 1, and 0·1 milligrammes; two died of general tuberculosis; two had a much less extensive disease at death.

3. *Culture Nine Months old.*—Three rabbits used; doses of 1, 1 and 0·1 milligramme. One died of accidental infection (Psorospermosis), the other two showed only a trace of tuberculosis when killed in 121 days.

4. *Culture Fourteen Months old.*—Three rabbits used; doses of 10, 10 and 1 milligramme, when killed in 89 days, only slight tuberculosis was seen.

A culture obtained from calf (797) inoculated with the original material was injected when two months old into four rabbits in doses of 10, 1·1, and 0·1 milligrammes. All the animals died of acute generalised tuberculosis.

The results show (*a*) the diminution of virulence of the culture obtained from the original material when subcultured, and (*b*) an increase of virulence for both calf and rabbit when the virus was passed through a calf.

These viruses therefore must be considered as showing an irregular virulence, an irregularity, indeed, which is not shown by the bovine viruses, nor by the virulent viruses of human origin. With Virus H. 49, "T.C.," there is evidence not only of the loss of virulence in the original culture by subculture, but an increase of virulence by passing the virus through the calf. Experiments with these viruses are still in progress.

INOCULATIONS WITH THE VIRUSES WHICH WERE AT FIRST SLIGHTLY VIRULENT AND SUBSEQUENTLY BECAME VIRULENT.

(Column IV. in Table.)

These are H. 17, "Sp. B." (Sputum), H. 13, "A.D." (bronchial gland tuberculosis), H. 21, "S.B." (bronchial gland) and H. 16, "J.H." (joint tuberculosis). These will be considered individually.

H. 17, "Sp.B." (*Sputum feeding*).

Sputum was used for feeding four calves, one for 91 days and the remaining three for 120 days.

First Calf.—The first calf (161) was killed in 125 days, and showed only minimal calcareous lesions in the ileum, in the pharyngeal and mesenteric glands, and one in a mediastinal gland.

An emulsion of the mesenteric and pharyngeal glands was injected into two calves in doses of 43,000 tubercle bacilli. These were killed in over 100 days. One showed no lesion, and the other showed D only.

The passage was not continued, and the dose of tubercle bacilli given was too small to decide on the virulence of the virus in the few experiments performed.

A culture from one of the calves, injected subcutaneously into two calves in 50 milligramme doses, produced only slight tuberculosis. It must be concluded, therefore, that at this time, at any rate, the virus was not virulent.

This is confirmed by the inoculations into rabbits, three of which were injected with doses respectively of 10, 1, and 0·1 milligrammes. Only slight tuberculosis was produced.

Second Calf.—One of the calves (167), fed for 120 days, showed only minimal calcareous lesions in the mesenteric glands.

By means of the emulsion of the affected glands the virus was passed through three sets of guinea-pigs.

An emulsion of the guinea-pig lesions, injected into one calf in a dose of 4·16 million subcutaneously, produced only a small local lesion, caseous nodules in the nearest lymphatic glands, and one in a bronchial gland, and 24 grey tubercles in the lungs.

The rabbits inoculated at the same time showed only slight tuberculosis.

From the calf emulsions were inoculated into two goats, producing much the same condition as was found in the calf itself. The dose in the goats was 102 million.

Rabbits inoculated with the same virus produced only slight tuberculosis.

Passage carried on from the goats into two other goats, in doses of 1 and 4 million tubercle bacilli, produced only minimal lesions of tuberculosis.

No experiments have yet been done with a culture of this strain obtained from Calf 391, so that as far as the passage has gone, we must conclude that the strain is not virulent.

Third Calf.—Another calf (171) showed only minimal calcareous lesions in the mesenteric glands after the feeding with sputum.

Passed on in a calf by an emulsion subcutaneously in the dose of 76,000 T.B., D only was produced, the lesions being chiefly calcareous.

Passed on from this calf to another calf in a dose of 400,000 T.B., only B was produced, and in a rabbit only slight tuberculosis.

This passage, therefore, is like the passage in the first calf; that is, the dose given was too small to completely test the virulence of the strain, although the slight tuberculosis produced in the rabbit would suggest that it was only slightly virulent.

Calf IV.

No experiments have been done with the culture.

Passage Experiment.

Fourth Calf.—The fourth animal (169) fed with sputum is the one from which a prolonged series of passage experiments was performed, and in which the virus, at first slightly virulent, became afterwards highly virulent.

Starting with the calf fed with sputum for 120 days, the lesions produced were a few minute calcareous foci in about one-third of the mesenteric glands, calcareous nodules in the pharyngeal glands, and many small tubercles in the small intestine.

First Passage: Subcutaneous. 390 days.

With the emulsion from these slight lesions rabbits inoculated showed only slight tuberculosis. These were not used for passage, but guinea-pigs inoculated at the same time showed general tuberculosis, and from these, other guinea-pigs were inoculated, and an emulsion of the organs of these was passed into a calf (339) subcutaneously, the dose being 165·8 million T.B. The calf was killed in 69 days; at the seat of inoculation was an ulcerated mass, and there was caseation of the prescapular and one pectoral gland, but no tuberculosis in the internal organs.

An emulsion of lesions of this animal was passed into guinea-pigs, so that the passage up to the present point consisted of the original animal, from which the strain was passed into two series of guinea-pigs successively, and then into another calf in a large dose, and then into guinea-pigs.

Up to this point the strain must be considered only slightly virulent, inasmuch as the rabbits injected with the emulsion showed only slight tuberculosis, and the calf, receiving a large dose, showed also slight tuberculosis.

Second Passage: Intravenous. 478 days.

An emulsion of the guinea-pig lesions was injected into two rabbits, producing only slight tuberculosis, and intravenously into a calf (475) in a dose of 104 million. The calf was killed in 88 days, and had progressing tuberculosis in the lungs, which showed nodules and softened areas, caseation of the prescapular glands, tuberculous iritis, and tubercles in the choroid.

The passage had now lasted 478 days, and from this animal, intravenously inoculated, the passage was continued successively and intravenously into three calves.

Third Passage: Intravenous.

The first calf (539) received 208 million and died in 18 days, showing miliary tuberculosis of the lungs.

Of two rabbits inoculated at the same time, one developed general tuberculosis (Rabbit 181) and the other moderate tuberculosis (intravenous injection). This effect in the rabbit is the first point in the passage in which the increase of virulence is shown, as one cannot accept in all cases the results of intravenous injection in bovines as a test of virulence of the strain—this is better gauged by subcutaneous injection.

The culture from Rabbit 181 presents distinctive features (see p. 92).

Fourth Passage: Intravenous. 509 days.

The next calf (529), intravenously injected from the previous intravenous inoculation received 1,021 million T.B. It died in 13 days and showed a progressing tuberculosis in the lungs and thoracic glands. The two rabbits inoculated at the same time both developed general tuberculosis.

Fifth Passage: Intravenous. 527 days.

The next calf (553) received intravenously 99 million T.B. It was killed when dying in 18 days. This was a smaller dose than the previous animal received, but it produced general miliary tuberculosis. The two rabbits inoculated at the same time developed general tuberculosis; the increased virulence of the strain for rabbits beink kept up.

The passage had now lasted 527 days.

Sixth Passage: Intravenous 586 days.

From the last intravenous injection an emulsion of the thoracic gland was injected subcutaneously into two calves (555) (531), and intravenously into Calf 557, and also into two rabbits. Both these rabbits died of general tuberculosis.

Seventh Passage: Intravenous.

Intravenous Injection.—The intravenous animal received 49·9 million T.B., and died in 17 days of tuberculous consolidation of the lungs and tuberculosis of the thoracic glands. Passed on intravenously into another calf (571) in a dose of 10 million T.B., the animal died in 26 days with general tuberculosis. Two rabbits were inoculated at the same time with 5 million T.B. (210 and 211); they died of general tuberculosis.

Looking at the table (Appendix) one sees that there are six animals in the series inoculated intravenously and that the last animal, which received the smallest dose, showed the greatest amount of tuberculosis; it lived the longest.

Subcutaneous Injection (sixth passage). Returning now to the animals subcutaneously inoculated in the sixth passage, each calf received 150 million T.B. in an emulsion of thoracic glands. They were both killed when dying in 58 and 59 days, and were found to have acute general tuberculosis.

The passage had lasted, up to this event, 586 days.

Looking at the whole series it must be concluded that at first, that is down to Calf 475 (the first intravenous injection, and second bovine passage) the strain was only slightly virulent for rabbits and for bovines. At this period the passage had lasted 478 days. After this the strain produced general tuberculosis in rabbits, the smallest dose given to a rabbit being 11 million, and the largest 1,225 million. At this time (2nd passage) there was some increase of virulence for calves; but the full virulence was not seen till later.

Cultures of the Passage.—We may now consider the experiments with the cultures which were obtained from this virus during the passage.

A culture was obtained from a guinea-pig (235) when the passage had lasted 390 days, and when the effect of the virus in rabbits and in one calf was only slight. This culture (Culture First Passage, Grade V., avirulent) was injected into two calves subcutaneously in 50 milligramme doses. It produced in 90 days only very slight tuberculosis in each animal.

Injected into rabbits intraperitoneally in doses of 50 milligrammes, 10 milligrammes, and 1 milligramme, it produced only slight tuberculosis.

It may be concluded, therefore, that at this stage the strain was only slightly virulent, both for bovines and for rabbits.

A culture was obtained from a rabbit (181) inoculated at the same time as the third in-intravenous injection (fourth passage), that is when the passage had lasted 509 days, and was classified by Dr. Eastwood as belonging to Grade 4. When 10 months old, the culture was injected into two calves in the dose of 50 milligrammes, and into three rabbits in doses of 10 and 1 milligrammes. It produced general tuberculosis in all the animals.

After 16 to 17 months culture (on blood serum), the culture when injected into 2 rabbits in a dose of 1 milligramme produced only slight tuberculosis, just like the slightly virulent human viruses.

There was therefore a distinct loss of virulence in a culture similar to the loss observed with the virus previously described (p. 36), H. 49 T.C., and this loss of virulence occurred in a culture obtained at a period of the passage when the virus was becoming virulent for calves.

A culture obtained from the last intravenous inoculation (seventh passage), injected subcutaneously into two calves in doses of 50 milligrammes, killed the animals in 33 and 37 days, respectively, with general tuberculosis.

Injected into two rabbits in doses of 10 and 1 milligrammes, both animals died of general tuberculosis.

This culture is unlike the two previous cultures. It belongs to Dr. Eastwood's Grade 1, and may therefore be called "Culture Seventh Passage, Grade I., Virulent."

The series of cultures in the passage are:—

Culture Grade V., avirulent, from the first bovine passage;

Culture Grade IV., irregular virulence, from the fourth bovine passage;

Culture Grade I., virulent, from the sixth and seventh bovine passages.

From the inoculation experiments it was seen that the strain was at first only slightly virulent for calves and rabbits, and that during the subsequent passage it was found virulent for both these animals.

(2) H 13, "A.D." (*Bronchial gland Tuberculosis*).

This was a case of tuberculosis occurring in a child four years of age, in which there was tuberculosis meningitis and general tuberculosis, in the from chiefly of miliary tuberculosis of the lungs and spleen. The bronchial glands contained caseating nodules. The intestines and mesenteric glands were normal. It may be considered as a somewhat familiar form of tuberculosis in children, which may be called "primary bronchial gland tuberculosis," and which ends not uncommonly with tuberculous meningitis and general miliary tuberculosis.

Experiment I.—For inoculation an emulsion was made of the bronchial glands and spleen, and two calves were injected subcutaneously with 16,000 T.B.

One calf (119) was killed in 67 days, and only showed a minimal tuberculosis.

An emulsion of these lesions, when injected into another calf (225) in a dose of 3·4 million T.B. produced in 89 days only a pea-sized calcareous local lesion.

This is a minimal result in both calves. No rabbits were inoculated and no cultures made, so that no further comment need be made on the result, except that, so far as it went, the experiment showed the strain to be only slightly virulent. It is particularly to be noted that a dose of 3·4 million T.B. produced only the slightest lesion in a calf.

Experiment II.—The second calf (129) which received 16,000 T.B. of an emulsion of the original material of the virus, showed in 66 days only a slight local lesion and some caseo-calcareous disease of the neighbouring glands.

An emulsion of these lesions was passed on into three series of guinea-pigs successively, and then passed (subcutaneously and intraperitoneally) into two calves (299, 301). Each calf received 541 million T.B. First Passage.

The one injected intraperitoneally was killed in 87 days, and showed tuberculous peritonitis, and tuberculosis of the thoracic and a few other glands. There was no disease of the internal organs.

The other calf (301), injected with the same dose subcutaneously, was killed when very ill in 33 days, and showed general tuberculosis.

A rabbit inoculated at the same time as C. 301 died of general tuberculosis.

A culture from Calf 301 was made and was found to be eugonic. It may be referred to as "Culture First Passage, Grade IV.; virulence irregular." The culture injected into 2 calves in a dose of 50 milligrammes produced in one general tuberculosis, and in the other only slight disease. In rabbits only slight disease was produced in one animal (1 milligramme) and general tuberculosis in two others (1 milligramme). The culture therefore showed irregular virulence.

From Calf 301 three calves were inoculated subcutaneously with an emulsion of the thoracic glands; two rabbits and two rats. First Passage.

Both rabbits died of general tuberculosis, and from one of the rats was obtained a culture which was found to be dysgonic, and may be called "Culture Second Passage, Grade I."

Of the three calves inoculated one (315) received 15,000 T.B., and showed in 70 days slightly more disease than the calves inoculated with an emulsion of the original material, which contained about the same number of bacilli.

The second calf (321), inoculated with 3·5 million T.B. was killed when very ill in 63 days, and was found to have general tuberculosis.

The third calf (325) which received 500 million T.B., in 24 days was found to have general tuberculosis.

The calf (321) which received 3·5 million T.B., was comparable with the calf already mentioned in Experiment I. (225), which had a similar dose, and developed only a slight local lesion.

From Calf 321 a culture was obtained which belongs to Grade I, and may be called "Culture, Grade I., Second Bovine Passage." This culture killed a calf in a dose of 50 milligrammes, and another calf in a dose of 10 milligrammes; a third calf with a dose of 10 milligrammes showed slighter disease than this but generalised. Two rabbits receiving 1 milligramme died of general tuberculosis.

With this virus the Culture First Passage was eugonic, and is to be classed in Grade 4 (in which no bovine strains occur) and showed irregular virulence, and the cultures obtained from the next passage were dysgonic, and classed in Grade I and were virulent for calves and rabbits.

(3) H 21, "G.B." (*Bronchial gland Tuberculosis.*)

The lesions used in this strain were obtained from a patient sixteen years old, who died of heart disease and pericarditis (not tuberculous). Tuberculous bronchial glands were discovered at the post-mortem examination, and were the only tuberculous lesions present. They consisted of eight or ten pigmented and congested glands, slightly enlarged, which showed on section a number of grey foci, containing tubercle bacilli. The bronchial glands were made into an emulsion, and injected into animals.

Two rabbits, each of which received 15,000 T.B. were killed in 97 days. One showed slight tuberculosis, and the other showed no tuberculosis.

One calf (285) received 157,000 T.B. subcutaneously. It was killed in 91 days, and no tuberculosis found.

The other calf (279), which received the same dose, also subcutaneously, showed a small local lesion and calcareous nodules in the prescapular gland, and the thoracic and one hepatic gland; three tubercles in the spleen.

An emulsion of these lesions was passed into two series of guinea-pigs successively, and from the guinea-pigs into two calves (first bovine passage), both subcutaneously. The dose given was, 4,797 million, and both animals were killed in 111 days. Second Passage.

One showed a small local lesion and calcareous grains in the prescapular gland.

The other (447) showed a fibrous local tumour, caseous foci in the nearest gland, calcareous grains in the thoracic glands, three small calcareous tubercles and one calcareous nodule in the lungs and small foci in one popliteal gland.

In both these cases the large dose of tubercle bacilli produced only small and degenerate lesions.

An emulsion of the prescapular gland of the last calf, injected into rabbits, produced only slight tuberculosis, and in guinea-pigs general tuberculosis.

Cultures.—Cultures were obtained from the calf (thoracic gland, 447), from one rabbit (155), and from one guinea-pig (417).

From the calf they were obtained direct from the posterior thoracic gland. Both rabbits were, as has been stated, inoculated from the prescapular gland.

The culture from the calf was eugonic, and in a dose of 50 milligrammes killed a calf in 24 days of general tuberculosis. General tuberculosis was produced in rabbits.

The culture from the guinea-pig was eugonic, and was injected into two calves in 50 milligramme doses.

One animal was killed in 90 days, and showed general tuberculosis. The other died in 55 days of general tuberculosis, and general tuberculosis was also produced in rabbits with this culture in doses of 0·01 and 10 milligrammes. The culture obtained from the rabbit, the source of which was the prescapular gland of the calf, has been found only slightly virulent for rabbits; a 10 milligramme dose produced only slight tuberculosis.

Dr. Cobbett thinks that the calcareous nodule in the lung of Calf 447 was possibly due to a case of spontaneous (inhalation) tuberculosis, and that the cultures obtained are possibly mixed, eugonic and dysgonic. No evidence on these points is forthcoming and no other even suspicious case of spontaneous tuberculosis has occurred among the bovines at Blythwood Farm. As however, some doubt might rest on the experiments with H. 21, G.B. it will be excluded from discussion.

(4) H 16, "J.H." (*Joint Tuberculosis.*)

The lesion from which the emulsion was obtained was from a case of chronic synovitis of the knee in a patient thirty-eight years of age. The material, which was removed by operation, consisted of swollen synovial membrane about 20 grammes in weight. In the cover-glass preparations of the emulsion only two tubercle bacilli were found.

Experiment I.—One calf (155) was inoculated subcutaneously with an emulsion containing 10,000 T.B. It was killed in 54 days, and only a small local lesion was found with slight affection of the neighbouring glands.

An emulsion of this local lesion and gland, passed subcutaneously into another calf in the dose of 713,000 T.B., showed in 91 days only a minimal calcareous lesion, and affection of the neighbouring glands.

The experiment ended at this point, and nothing further need be said about it. It is not conclusive as to the virulence of the strain, as only very small doses were used.

Experiment II.—Another calf (157) received the same dose of the emulsion of the original material as in Experiment I. (10,000 T.B., subcutaneously), and was killed in 67 days. It showed the same lesions as the Calf in Experiment I., with the exception that there was one calcareous focus in the right bronchial gland.

First Passage: Subcutaneous.

An emulsion of the prescapular gland of this calf, injected into another calf (187) subcutaneously in the dose of 3 million T.B., produced in 81 days only a minimal calcareous lesion.

Second Passage: Subcutaneous.

An emulsion of the local lesion and gland was passed into another calf (273) in the dose of 10·9 million T.B. subcutaneously. This calf was killed in 89 days, and besides a local lesion and disease of the prescapular gland, it showed many tuberculous nodules in the lungs, and some tuberculosis of the liver and spleen, thoracic and hepatic glands, and one parotid lymphatic gland. These were the lesions of an extending tuberculosis, and were unlike the calcareous foci which were found in the two previous calves.

The three calves already mentioned were injected with an increasing dose (10,000, 3 million, 10 million).

Third Passage: Subcutaneous.

An emulsion of the prescapular gland of the second passage was injected into one rabbit (39), which died of general tuberculosis, and into two calves subcutaneously in doses of 3 million T.B.

One calf (355) died of general tuberculosis in 43 days; the other calf (337) was killed in 80 days, and showed a generalised progressing disease, not so acute as in the first calf.

This third bovine passage, in which general tuberculosis was produced, contrasts with the first bovine passage, in which the same dose produced only a minimal local lesion.

Fourth Passage: Subcutaneous,

From one of the calves (337) of this passage an emulsion of the prescapular gland was injected into four calves and two rabbits. The two rabbits died of general tuberculosis.

The four calves received doses of 10,000, 712,000, 3 million, and 10 million T.B., doses previously given during the passage.

The one (371) that received the smallest dose was killed in 66 days, and showed a progressing caseous tuberculosis. This is the same dose of bacilli as the calf injected with an emulsion of the original material, which showed slight tuberculosis only.

The other three calves (343, 317, 281) died of general tuberculosis. One calf (317) received the same dose as the calf in the first bovine passage, which showed only a minimal lesion, and another (281) received the same dose as the calf in the second bovine passage, and showed general tuberculosis, while the other (273) showed a general tuberculosis not so acute. The third calf (343) received the same dose as a calf in Experiment I., which showed minimal lesions.

Fifth Passage: Subcutaneous.

From the rabbits of this series one calf (423a) was injected subcutaneously with 157 million T.B. It was killed very ill in 42 days, and showed general tuberculosis.

An adult bovine (245) received the same dose subcutaneously. It was killed in 209 days, and showed extensive and active tuberculosis.

Cultures of the Passage.

The cultures which were obtained from this strain during the passage are as follows:—

Original Material.—Two cultures were obtained from animals inoculated with the original material, one from a guinea-pig and one from a calf (157). Both these cultures belong to Dr. Eastwood's Grade V. Grade V. contains no bovine strains

A culture from the guinea-pig was injected into two calves, each of which received a dose of 50 milligrammes. They were killed in 90 days, and showed slight tuberculosis. Injected into rabbits in doses of 10, 1, and 0·1 milligrammes only slight tuberculosis was produced.

The culture from the original material must therefore be considered as only slightly virulent for calves and rabbits in the doses used. This culture may be referred to as "Culture, of original material, Grade V., avirulent."

Second Passage.—The next culture was obtained from the second bovine passage (C. 273) and is also to be classed in Grade V.

Injected into two calves in doses of 50 milligrammes in 90 days only slight tuberculosis was produced. Injected into rabbits in doses of 10, 1, and 0·1 milligrammes only slight tuberculosis resulted.

The calf (273) from which this culture was obtained showed spreading but not acute tuberculosis. This culture may be called "Culture second bovine passage, Grade V., avirulent."

Third Passage.—The next culture was obtained from the third bovine passage (Calf 337). It is classified in Grade III.

Injected into two calves in doses of 50 milligrammes, general tuberculosis was produced. Injected into rabbits in doses of 10, 1, and 0·1 milligrammes, five animals in all, it produced general tuberculosis.

This culture may be called "Culture, third bovine passage, Grade III., moderately virulent."

Fourth Passage.—A culture from this passage (Calf 317) produced general tuberculosis in calves and rabbits. It is dysgonic, and may be called "Culture, fourth bovine passage, virulent." This culture has not lost its virulence, although subcultured for a long period both on serum and serum glycerine.

Fifth Passage.—The fifth culture was obtained from the fifth bovine passage, and is classified in Grade 1, being typically dysgonic.

Injected into each of two calves in doses of 50 milligrammes it caused death in 25 and 39 days with general tuberculosis. Injected into rabbits in doses of 10, 1, and 0·1 milligrammes, it produced general tuberculosis in all the animals.

This culture may be called "Culture, fifth bovine passage, Grade 1, virulent."

The series of cultures obtained from the animals during the passage in the three strains are shown in the following table:—

—	H. 17, "Sp. B."	H. 13, "A D"	H. 16. "J.H."
Culture from Original Material	—	—	Grade V., avirulent.
Culture from First Bovine Passage	Grade V., avirulent	Grade IV., virulence irregular.	—
Culture from Second Bovine Passage -	—	Grade I., virulent	Grade V., avirulent.
Culture from Third Bovine Passage - -	—	—	Grade III., virulent.
Culture from Fourth Bovine Passage -	Grade IV., virulence irregular.	—	Dysgonic, virulent.
Culture from Fifth Bovine Passage -	—	—	Grade I., virulent.
Culture from Sixth Bovine Passage	Grade I., virulent	—	—
Culture from Seventh Bovine Passage	Grade I., virulent	—	—

This table shows clearly, more particularly in the case of prolonged passage of H. 17, Sp. B. and H. 16, J.H., that during the passage the culture obtained from the lesion produced is at first luxuriant in its growth and avirulent and that later in the passage the culture obtained grows less luxuriantly and is virulent; passing from the type of bacillus, slightly virulent and eugonic, which is obtained from many lesions in the human subject to the dysgonic virulent type which is obtained from tuberculous lesions in bovines. The transformation in the case of these two viruses was slow: it was more rapid in the case of H. 13, "A.D.," and still more rapid in the case of a virus already discussed, H. 49, "T.C." (p. 89).

The results with the three strains just considered may be compared with other cases of passage, which have been maintained by tissue emulsions of slightly virulent strains. The results are shown in the following Table:—

Strain.	No. of Bovine Passages.	Duration in Days.	Result.
Pulmonary Tuberculosis :—			
H. 1, "C.M."	3	344	Minimal lesions.
H. 22, "F.W."	4	240	(See results of intravenous injection, p. 21.)
H. 23, "J.P"	2	143	Original material caused slight generalisation of disease.
H. 25, "A.T."	(twice over) 1	127	Some extension of disease in first passage.
Mesenteric Glands :—			
H. 8, "S.C."	6	222	Intravenous. (First and third passage) caused lesions.
H. 12, "H.N."	4	356	Small extension of disease, third passage.
H. 18, "T.T."	3	306	Small extension of disease, second passage.
Joints :—			
H. 11, "E.D."	4	408	Minimal lesions.
H. 15, "I.W."	4	231	Caseous tubercle. (Second passage.)

These experiments do not show the increase of virulence by passage observed in the cases previously considered.

The interpretation to be placed on these passage experiments, in which increase of virulence is shown, is of very great importance.

(*a*) One view which may be stated is that the slightly virulent bacillus of the human lesion, by its passage through bovines, has lost its eugonic character of growth, and has become dysgonic and virulent. This view would necessitate the supposition that the eugonic slightly virulent human bacillus has been transformed by passage in the bovine into a virulent bacillus indistinguishable from that obtained from bovine lesions.

(*b*) Another view, however, must be considered, and it is this. It might be supposed that the original lesion in the human being was produced by the human bacillus, but that this lesion also contained the bovine bacillus, either as a "harmless lodger" or as an "active partner." In any case the emulsion of the original material which is injected into the calf might be supposed to contain two kinds of bacilli, the human and the bovine, the former bacillus being in excess.

The argument may be illustrated by taking Virus H. 16, "J.H." as an example. The two kinds of bacilli, injected with the original material into the first calf, would produce a minimal lesion, the eugonic bacillus being in excess. The culture obtained from this lesion contains the eugonic human bacillus still in a large preponderance over the bovine bacilli, and when injected in the first bovine passage would still produce a minimal lesion. Injected (by culture) into a calf at the second bovine passage a greater degree of tuberculosis is produced, because the eugonic bacilli are dying out, and the bovine bacilli are becoming more numerous, as they have a suitable soil. Still the culture contains a preponderance of the eugonic bacilli, and is classified in Grade V. In the third bovine passage the same is occurring, with still further loss of the eugonic bacilli, so that now the dysgonic bovine bacilli are chiefly present, and the disease produced is a generalised tuberculosis. This is still more marked in the fourth and fifth bovine passage, in which the eugonic bacilli have completely disappeared, and the culture produced belongs to Grade 1, and is what may be considered as a typically bovine bacillus. In both these passages the result is a general tuberculosis from the inoculation of the bacilli in the doses given.

The result in the rabbits follow closely the results in the calves as regards the virulence of the bacilli.

Experiments are still being conducted to determine which of these views is correct.

The questions involved in this discussion are:—

1. As to whether the bovine bacillus is a completely distinct micro-organism from the tubercle bacillus producing the human lesions, in the sense that the bovine bacillus which produces bovine tuberculosis, does not produce human tuberculosis in the human being, and that the human bacillus, which produces human tuberculosis, does not produce bovine tuberculosis in the bovine.

2. The bovine bacillus might conceivably be found in tuberculous lesions in the human being, having been accidentally introduced, but it does no material harm. An emulsion or even a culture, from any human tuberculous lesion, might contain both kinds of bacilli.

GENERAL SUMMARY OF RESULTS.

1. *Bovine Tuberculosis.*

(Thirty strains examined.)

The bacillus of bovine tuberculosis has been shown by the experiments to have certain characteristics as follows:—

α. It shows some variations in its growth on artificial media and according to these variations can be arranged into three groups or grades (I., II., III.).

β. When inoculated into bovines, rabbits, guinea-pigs, pigs, goats, monkeys and the chimpanzee in appropriate doses it produces death by generalised tuberculosis.

γ. It shows stability as regards its cultural characters, both when subcultured and when passed through animals. Whether these characters can be altered by prolonged passage in certain animals is still the subject of experiment and cannot now be answered.

δ. It shows great stability in virulence both after long subcultivation and after passing through animals.

2. *Human Tuberculosis.*

(Sixty cases examined.)

The bacilli of human tuberculosis show a greater variety than those of bovine tuberculosis.

Group I.

(Fourteen cases examined.)

α. The bacilli obtained from the virus of human beings in this group have all the characters of the bacillus of bovine tuberculosis as regards cultural characters, virulence for the animals previously mentioned, and stability of cultural characters and of virulence.

The bacillus of this Group is identical with the bacillus of bovine tuberculosis.

β. The bacillus of these cases was a single bacillus—there was no evidence of a "mixture" of different kinds of bacilli.

γ. The bacillus was the cause of death of the individuals from which it was obtained. This is more particularly shown by the study of Viruses H. 32 "Y.W.," H. 59 "L.B." and H. 64 "M.G." in which general tuberculosis was the cause of death of the child. The disease started as abdominal tuberculosis, but became generalised. Culture not only from the mesenteric glands, but also from the bronchial glands and lungs and meninges had the characteristics of the bovine bacillus in cultivation and in virulence. No mixture of bacilli was here present. The children died of an infection by the bacillus of bovine tuberculosis.

This Group includes three cases of cervical gland tuberculosis and eleven cases of abdominal tuberculosis.

Group II.

(Forty cases examined.)

The bacilli obtained from the virus of human tuberculosis in this group differs from the bacillus of bovine tuberculosis in the following points:

α. In culture they are more luxuriant and are distinguished as referable to Groups IV. and V.

β. When inoculated into calves and rabbits they do not produce the generalised and fatal disease caused by the bovine bacillus.

The result of inoculation is not a negative one, but varies within certain limits with different viruses, and in rabbits the viruses occasionally kill the animal by producing a generalised disease.

They agree with the characteristics of the bovine bacillus in the following points:

α. They produce general tuberculosis in monkeys and the chimpanzee.

β. The lesions produced in these animals are the same anatomically as those produced by the bovine bacillus.

γ. The lesions produced in calves and rabbits are histologically tuberculosis, although usually they show retrogression.

This group includes:—

Sputum Culture	2 cases.
Pulmonary Tuberculosis	10 ,,
General ,,	1 ,,
Bronchial Gland ,,	2 ,,
Cervical Gland ,,	6 ,,
Abdominal ,,	8 ,,
Joint ,,	9 ,,
Testicle ,,	1 ,,
Kidney ,,	1 ,,

The experiments show, however, that this division into two groups of the bacilli found in human tuberculosis is not the whole question.

Group III.

(Six cases examined.)

The investigation of two viruses, H. 53, "D.H." and H. 49, "T.C." (p. 89) shows that bacilli are obtainable from cases of human tuberculosis which belong to neither group. The bacilli from the two viruses mentioned showed an irregular virulence in calves and rabbits, and one of them, H. 49, "T.C." showed also (1) that the culture of the original material lost its virulence after prolonged subcultivation and (2) that the original virus although irregularly virulent for calves became highly and uniformly virulent after being passed through a calf. The culture of H. 49, "T.C." obtained from the original material has in cultivation the characters of the bacillus of bovine tuberculosis, belonging to Grade II. There was no evidence of mixture in the case of either viruses.

The results of the examination of the bacilli in the case of these two viruses points to the conclusion that the bacilli were bovine in origin and had been altered by residence in the human being.

As bearing intimately on this matter, the question of the transformation of the human bacillus into the bovine as shown in the experiments previously discussed (p. 90) must be mentioned.

When by passage through calves, the slightly virulent bacillus of human tuberculosis becomes apparently modified into the bovine bacillus, it was suggested that it was not a real modification, but that the original virus was a mixture of bacilli, and that during the passage the bovine bacillus alone survived. But in these passage experiments there is evidence that at the time when the virus is becoming virulent, the bacilli separated by culture are "unstable" in virulence for calves and rabbits; an instability similar to that of the original virus of H. 49, "T.C."

The consideration of these cases tends to bridge the gap between the bacilli of Group I. (bovine bacilli) and those of Group II., which they suggest may only be a form of bovine bacillus, degraded as regards virulence for calves and rabbits, by long residence in the human body.

Sidney Martin.

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OF THE

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APPOINTED TO INQUIRE INTO THE RELATIONS OF

HUMAN AND ANIMAL TUBERCULOSIS

PART I.

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THIRD INTERIM REPORT

OF THE

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APPOINTED TO INQUIRE INTO THE RELATIONS OF

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REPORT AND APPENDIX.

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NEW ROYAL COMMISSION ON TUBERCULOSIS.

EDWARD R.

EDWARD THE SEVENTH, by the Grace of God of the United Kingdom of Great Britain and Ireland, King, Defender of the Faith, To

Our Trusty and Well-beloved Sir MICHAEL FOSTER, Knight Commander of Our most Honourable Order of the Bath, Doctor of Medicine, Fellow of the Royal Society, Professor of Physiology in Our University of Cambridge ;

Our Trusty and Well-beloved GERMAN SIMS WOODHEAD, Esquire, Doctor of Medicine, Professor of Pathology in Our University of Cambridge ;

Our Trusty and Well-beloved SIDNEY HARRIS COX MARTIN, Esquire, Doctor of Medicine, Fellow of the Royal Society, Professor of Pathology at University College, London ;

Our Trusty and Well-beloved JOHN MCFADYEAN, Esquire, Principal and Professor of Comparative Pathology and Bacteriology at the Royal Veterinary College ; And

Our Trusty and Well-beloved RUBERT WILLIAM BOYCE, Esquire, Professor of Pathology at University College, Liverpool.

GREETING :

Whereas We have deemed it expedient that a Commission should forthwith issue to inquire and report with respect to Tuberculosis :—

1. Whether the disease in animals and man is one and the same ;
2. Whether animals and man can be reciprocally infected with it ;
3. Under what conditions, if at all, the transmission of the disease from animals to man takes place, and what are the circumstances favourable or unfavourable to such transmission.

Now know ye, that We, reposing great trust and confidence in your knowledge and ability, have authorised and appointed, and do by these Presents authorise and appoint you, the said Sir Michael Foster, German Sims Woodhead, Sidney Harris Cox Martin, John McFadyean, and Rubert William Boyce, to be Our Commissioners for the purposes of the said inquiry.

And for the better effecting the purposes of this Our Commission We do by these Presents give and grant unto you, or any three or more of you, full power to call before you such persons as you shall judge likely to afford you any information upon the subject of this Our Commission ; and also to call for, have access to, and examine all such books, documents, registers, and records as may afford you the fullest information on the subject, and to inquire of and concerning the premises by all other lawful ways and means whatsoever.

And We do by these Presents authorise and empower you, or any three or more of you, to visit and personally inspect such places as you may deem it expedient so to inspect for the more effectual carrying out of the purposes aforesaid.

And We do further by these Presents will and ordain that this Our Commission shall continue in full force and virtue, and that you, Our said Commissioners, or any three or more of you, may from time to time proceed in the execution thereof, and of every matter and thing therein contained, although the same be not continued from time to time by adjournment.

And We do further ordain that you, or any three or more of you, have liberty

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to report your proceedings under this Our Commission from time to time if you shall judge it expedient so to do.

And Our further Will and Pleasure is that you do, with as little delay as possible, report to Us under your hands and seals, or under the hands and seals of any three or more of you, your opinion upon the matters herein submitted for your consideration.

Given at Our Court at St. James's the Thirty-first day of August, 1901; in the first Year of Our Reign.

By His Majesty's Command.

CHARLES RITCHIE.

EDWARD R. & I.

EDWARD THE SEVENTH, by the Grace of God, of the United Kingdom of Great Britain and Ireland and of the British Dominions beyond the Seas King, Defender of the Faith, To

Our Trusty and Well-beloved WILLIAM HENRY POWER, Esquire, Companion of Our most Honourable Order of the Bath, Fellow of the Royal Society, Medical Officer of the Local Government Board,

GREETING:

Whereas by Warrant under Our Royal Sign Manual, bearing date the Thirty-first day of August, one thousand nine hundred and one, We were pleased to appoint Commissioners to inquire and report with respect to Tuberculosis, and to authorize the late Sir Michael Foster to act as Chairman of the Commission:

And whereas the Chairmanship of the Commission is at this present void.

Now know ye that We, reposing great trust and confidence in your knowledge and ability, have authorized and appointed, and by these Presents authorize and appoint you, the said William Henry Power, to be Chairman of the said Commission in the room of the said Sir Michael Foster, deceased.

Given at Our Court at Saint James's the Eighteenth day of March, 1907; in the seventh Year of Our Reign.

By His Majesty's Command.

H. J. GLADSTONE.

TO THE KING'S MOST EXCELLENT MAJESTY.

May it please your Majesty,

We, your Majesty's Commissioners, appointed to inquire and report with respect to Tuberculosis :—

1. Whether the disease in animals and man is one and the same ;
2. Whether animals and man can be reciprocally infected with it ;
3. Under what conditions, if at all, the transmission of the disease from animals to man takes place, and what are the circumstances favourable or unfavourable to such transmission ;

humbly submit the following Further Report containing an account of certain experiments we have carried out regarding the Infectivity of the Milk and Faeces of Naturally Infected Tuberculous Cows, that is, Cows that had contracted the disease in the ordinary way.

We wish to take this opportunity of expressing our deep sense of the great loss caused not only to ourselves but also to the whole country by the lamented death of Sir Michael Foster, the late Chairman of this Commission.

Since the date of our Second Interim Report the work of the Commission has been mainly directed to determining the special characters of the bacilli which are the cause of tuberculosis in animals other than the cow, and the relationships of the different types of tubercle bacilli which we have encountered in man and certain of the lower animals. The investigations bearing on these and other matters referred to in that Report as engaging our attention are not yet complete and the publication of the results obtained must therefore be postponed.

In the meantime we have thought it advisable to describe the results of a series of experiments which have been carried out by us with a view of obtaining information regarding the excretion or discharge of tubercle bacilli in the Milk and Faeces of tuberculous cattle.

In our Second Interim Report we expressed the opinion, as a result of our investigations, that a very considerable amount of disease and loss of life, especially among infants and children, must be attributed to the consumption of cow's milk containing tubercle bacilli.

Tuberculosis involving the udder is comparatively common in cows, and in such cases their milk always contains tubercle bacilli and is therefore dangerous for human beings consuming it. It was, however, undecided what is the danger, if any, attaching to the milk of tuberculous cows in which the udder presents no evidence of disease. We therefore took the opportunity of making a number of observations and experiments bearing on this point. The experiments were made with the milk of cows which had contracted the disease in the natural way.

In natural tuberculosis in the cow, cases which show such obvious symptoms of the disease as emaciation and cough should be considered separately from the cases in which there are no such signs and in which the disease is to be recognised during life only by means of the injection of tuberculin.

None of the cows investigated showed any sign of disease of the udder during life, and in all, after slaughtering, the udder was carefully examined for tuberculous lesions and tubercle bacilli. No tuberculosis was found except in one case (Cow F) in which one quarter of the udder showed four small nodules. These could not possibly have been detected during life.

We found that the milk of the cows obviously suffering from tuberculosis (*see* Appendix ; Cows B, C, and F) contained tubercle bacilli whether the milk was obtained in the ordinary way or was withdrawn from the teat by means of a sterilised catheter. The presence of tubercle bacilli in the milk of cows clinically recognisable as tuberculous confirms the opinion we expressed in our Second Interim Report that the milk of such cows must be considered dangerous for human beings.

The experiments which we have carried out with regard to the infectivity of the faeces of tuberculous cows were dictated by knowledge of the fact that dirt of various kinds from cows and the cow-shed is almost constantly present in milk as it reaches the consumer. Cows suffering from extensive tuberculosis of the lungs must discharge considerable numbers of bacilli from the air passages in the act of coughing, and some of the bacilli thus expelled may find their way into the milk. But our experiments indicate that the excrement of cows obviously suffering from tuberculosis of the lungs or alimentary canal must be regarded as much more dangerous than the matter discharged from the mouth or nostrils. We have found that even in the case of cows with slight tuberculous lesions tubercle bacilli in small numbers are discharged in the faeces, while as regards cows clinically tuberculous our experiments show that the faeces contain large numbers of living and virulent tubercle bacilli.

The presence of tuberculous cows such as B, C, and F in company with healthy cows in the cow-shed is therefore distinctly dangerous, as some of the tubercle bacilli which escape from their bodies in the excrement are almost certain to find their way into the milk.

The experiments are described in detail in the Appendix attached to this Report. They were carried out by Dr. F. Griffith under our supervision, and we desire to express our high appreciation of the skill and care devoted by him to the work.

(Signed) W. H. POWER, *Chairman.*
G. SIMS WOODHEAD.
SIDNEY MARTIN.
J. McFADYEAN.
RUBERT BOYCE.

EDWARD J. STEEGMANN, *Secretary.*

January, 1909.

APPENDIX

BY

Dr. F. GRIFFITH.

INTRODUCTION.

THIS Appendix gives the results of inoculation and feeding experiments made with the faeces and milk of naturally tuberculous cattle. Observations have been made on six milch cows. Three of the animals, B, C, and F, showed clinical evidence of tuberculosis but in none during life could any tuberculous disease of the udder be detected. The object of this investigation was to ascertain if tubercle bacilli were present in the faeces and milk of these animals.

DESCRIPTION OF METHODS USED.

For the purposes of the experiments a considerable quantity of faecal matter was required, and in order to avoid risk of contamination from the genito-urinary passages the following method of collection was employed. The action of the rectum was stimulated by the injection into it of air through a sterile glass tube and the faeces were received directly into a pail which was applied to the margin of the anal orifice. These precautions were necessary as in one case, B, there was a purulent discharge from the vagina and the post-mortem examination in three cases, B, C, and F, revealed extensive tuberculous disease of the uterus. A portion of the faeces was rubbed up in a mortar with sufficient salt solution to moisten it and pressed through muslin to form an emulsion. This emulsion was used for the feeding and inoculation of guinea-pigs. The inoculation of fresh faeces into guinea-pigs frequently causes death within a few days and it was possible to estimate roughly a minimal fatal dose of the emulsion which was prepared each day in the same way. It was found that 0·5 cubic centimetre of the emulsion almost invariably caused death from acute peritonitis while after the inoculation of 0·05 cubic centimetre all the animals survived. The intraperitoneal method of inoculation was almost exclusively used.

The infectivity of the faeces was also tested by feeding guinea-pigs and swine. The swine were young animals about 11 weeks old, belonging to three litters and all obtained from the same farm. They were all tested with tuberculin before being used for experiment and gave negative results in each case. Two animals were kept as controls, one from each of two litters, and when killed were found to be free from tuberculosis. No control to the third litter was kept, but all the eight pigs belonging to it though used for experiment were quite healthy when killed.

The milk of five of the cows, B, C, D, E, and F, was tested for the presence of tubercle bacilli and strict precautions were taken to ensure absence of contamination during its collection. A metal catheter, connected by pressure tubing to a flask, was inserted into the milk sinus of the udder, a separate apparatus being used for each quarter, and the milk was withdrawn from the udder by the exhaustion of the air in the flask. Before the insertion of the catheter each teat was washed with a solution of perchloride of mercury and with methylated spirit, and the opening was inspected to ensure that no faecal matter was pushed in with the catheter.

The milk thus obtained was tested as to the presence in it of tubercle bacilli by the inoculation of guinea-pigs and occasionally of rabbits. Two guinea-pigs were inoculated intraperitoneally from each quarter and each animal received, when sufficient milk was obtained, a dose of 10·0 cc. of uncentrifuged milk plus the deposit of 20·0 cc. of centrifuged milk, or sometimes 6·0 cc. plus the deposit of 24·0 cc.

In the case of three cows young swine were fed in each instance with the milk from the different quarters mixed together.

DETAILS OF THE EXPERIMENTS.

1. Animals showing clinical signs of disease.
2. Animals in which the only evidence of disease during life was a positive reaction to tuberculin.

1.

COW B.

This cow was a shorthorn and had calved four weeks previously. It was in poor condition and had a short infrequent cough; it reacted positively to the tuberculin test.

When killed it was found to have severe general tuberculosis. The lungs contained caseous masses which had broken down and had become partly emptied with the formation of cavities. There were numerous tubercles along the whole length of the trachea and the tonsils were infiltrated with breaking down caseous tissue. In the small intestine there were about 60 ulcers varying up to 1·5 cubic centimetre in diameter and scattered caseous nodules not yet ulcerated. The bronchial, mediastinal, mesenteric and portal glands were greatly enlarged and replaced by firm caseo-necrotic tissue. The posterior pharyngeal, and the cervical glands were large and extensively caseated. The walls of the uterus were thick, firm, and infiltrated with tuberculous tissue, while the cavities were filled with muco-purulent discharge such as issued from the vagina during life. The udder was free from tuberculous lesions.

The calf from this animal was in good condition and apparently healthy, but the post-mortem examination revealed disseminated tuberculosis. It was evident from the distribution of the disease (see post-mortem), and its extent in relation to the age of the calf, that the tuberculosis had been acquired in utero. That the cow had been able to bear a calf is remarkable considering the advanced tuberculous disease of the uterus, though probably the pregnancy itself had hastened the progress of the disease.

Inoculation and Feeding Experiments with Faeces.

The faeces of Cow B passed on the 1st, 3rd, 4th, 5th, 8th, and 9th of October, 1907, were tested for the presence of tubercle bacilli by the inoculation of guinea-pigs.

In all 25 guinea-pigs were inoculated intraperitoneally, of which 8 succumbed to acute infection in from one to two days. One, killed after 27 days, was free from tuberculosis. The remaining 16 were killed after about four weeks and were found to be tuberculous — that is, all the guinea-pigs with one exception inoculated with faeces which lived for a sufficient period for tuberculosis to develop became tuberculous. The doses in relation to the amount of faeces passed were exceedingly small, consisting in the majority of cases of ·05 cc. of a thick filtered emulsion.

Guinea-pigs were also fed with the faeces. Six were fed from October 1st to October 9th inclusive with faeces mixed with sterilized milk, receiving no other food, and when killed were healthy.

Two guinea-pigs were fed each day from October 1st to October 9th, sixteen in all, with a single dose of faeces administered by means of a pipette, each receiving 1·0 cc. of the emulsion used for the intraperitoneal inoculations. They were killed after 14 weeks and were free from tuberculosis in spite of the fact that they received 50 times the amount of faecal emulsion which invariably caused tuberculosis when inoculated intraperitoneally.

Four young swine were fed with faeces mixed with sterilized milk from October 1st to October 9th, 1907, the total amount shared between the four from the same trough being 19·1 kilogrammes. They were tested with tuberculin 58 days after the experiment began and all gave positive reactions, the rise of temperature varying in the individual cases from 1·3° C. to 3·0° C. They were killed after periods varying from 63 to 100 days since the first feeding, and all showed generalized tuberculosis (see post-mortem records).

INOCULATION AND FEEDING EXPERIMENTS WITH MILK.

The milk of Cow B, collected in the manner previously described, was inoculated into guinea-pigs on the 11th, 14th, 15th, 16th, 17th, 18th, and 19th of October, 1907. The inoculations were all made intraperitoneally, and two guinea-pigs were used for the milk of each quarter, each animal receiving a dose consisting of the deposit of 20·0 cubic centimetres of centrifuged milk plus 10·0 cubic centimetres of uncentrifuged milk (except on the first day when each received the deposit of 15·0 cubic centimetres).

In all 56 guinea-pigs were inoculated. One was killed in 79 days and had general tuberculosis without disease of the omentum. In these experiments I have not accepted tuberculosis in a guinea-pig as giving positive evidence of the presence of tubercle bacilli in the material inoculated unless there were lesions in the omentum, muscle, or skin at the seat of inoculation containing tubercle bacilli, and therefore this guinea-pig was rejected. The remaining 55 guinea-pigs were killed, the majority after 11 weeks, and all were healthy with the exception of one which had tuberculosis obviously due to the inoculation.

On November 5th, 1907, the cow was inoculated with 20·0 cubic centimetres of tuberculin under the skin of the neck after which she became ill, with laboured breathing. The next day, 19 hours later, the milk was inoculated as before into eight guinea-pigs of which four subsequently became tuberculous. The milk collected on November 7th, 43 hours after the inoculation of tuberculin, caused tuberculosis in seven out of the eight guinea-pigs inoculated.

Two young pigs were fed from October 14th to October 20th inclusive, receiving between them 18·4 litres of milk. They were killed 86 days after the first feeding and showed no tuberculosis. A third pig, which received on November 1st a single feed of 2·8 litres of milk, when killed 69 days later was healthy.

The following experiments were performed in order to gain information as to the likelihood of the milk becoming infected during the ordinary process of milking.

On November 4th, the cow was milked in the ordinary way, though with special precautions as to cleanliness, into an open pail; two out of four guinea-pigs inoculated with the mixed milk became tuberculous.

On November 5th, before the tuberculin inoculation, the cow was milked without being cleansed in any way: two out of four guinea-pigs inoculated with the mixed milk became tuberculous.

The experiments are not conclusive since it is possible that the tubercle bacilli were excreted in the milk, although use of it on seven separate occasions two or three weeks previously had caused tuberculosis in one guinea-pig only. In an animal so severely infected as this cow an invasion of the blood stream by tubercle bacilli is always liable to occur and these may be eliminated in the milk.

This natural distribution of tubercle bacilli in the course of the disease may account for the presence of tubercle bacilli in the milk after the inoculation of tuberculin, this inoculation being coincident with and not the cause of the dissemination.

COW C.

This cow was a Jersey with obvious clinical signs of tuberculosis. She was emaciated and feeble, breathed hard, and had a frequent cough. Her temperature was febrile and there was no rise sufficient to constitute a positive reaction after the inoculation of tuberculin. After death she was found to have severe thoracic tuberculosis: the lungs were closely beset with caseous nodules and large bright yellow caseo-necrotic masses, many of which were softening and breaking down. In several cases caseo-purulent substance was seen protruding from a necrotic mass into a bronchus and the trachea was filled with a cast of inspissated muco-pus. The bronchial and mediastinal glands were greatly enlarged and caseo-necrotic throughout. The Peyer's patches of the small intestine all contained a few caseous nodules up to a hemp-seed in size, and there were several small ulcers up to 5·0 millimetres in diameter. One mesenteric gland was greatly enlarged and caseous. The uterus was extensively tuberculous and the cavities were filled with purulent fluid and caseous flocculi. The udder was normal.

INOCULATION AND FEEDING EXPERIMENTS WITH FAECES.

The faeces of Cow C were tested for the presence of tubercle bacilli on the 24th, 25th, 28th, 29th, and 30th of October, 1907, by the inoculation of 30 guinea-pigs. Of these 17 became tuberculous : the rest died too soon for tuberculosis to develop.

Four guinea-pigs were fed continuously for six days with faeces mixed with sterilized milk : one became tuberculous, the rest remained healthy.

Each of ten guinea-pigs received by the mouth from a pipette 1·0 cubic centimetre of the faecal emulsion used for the inoculation experiments, and when killed after about 90 days all were found to be free from tuberculosis.

The following experiment gives some idea of the large numbers of tubercle bacilli in the faeces of this cow. One gramme of faeces was added to two litres of sterilized water, and two guinea-pigs were inoculated intraperitoneally, one with one cubic centimetre, the other with two cubic centimetres of the mixture. Both developed severe general tuberculosis, the former dying in 63 days.

A young pig was fed with the faeces from October 23rd to October 30th inclusive, receiving 5·56 kilogrammes mixed with sterilized milk. It was killed 48 days after the first feeding and showed enlargement and caseation of the submaxillary and mesenteric glands and disseminated tuberculosis.

INOCULATION EXPERIMENTS WITH MILK.

The milk was collected by catheter on each of three days and was inoculated intraperitoneally into guinea-pigs and rabbits. Each guinea-pig received 10·0 cubic centimetres of uncentrifuged milk added to the deposit of 40·0 cubic centimetres of centrifuged milk.

None of the animals inoculated on October 25th became tuberculous. The milk of October 29th caused tuberculosis in two guinea-pigs and that of October 30th caused tuberculosis in three rabbits and four guinea-pigs. The infectivity of the milk with reference to the individual quarters was irregular, but each quarter at some time gave tuberculous milk.

The explanation of this fact may be that the quantity of milk inoculated was not sufficient to be representative rather than that the elimination of tubercle bacilli was irregular, since in several of the animals the slight amount of disease produced showed that only a few bacilli had been inoculated.

COW F.

This animal was very ill : she was emaciated and feeble, and was kept under observation only for a few days, after which she was killed.

The post-mortem examination revealed severe general tuberculosis apparently originating in the alimentary tract. In the left hind quarter of the udder, in the tissue forming the wall of the main sinus near the teat, there were four reddish grey caseating nodules up to a pea in size. The rest of this quarter and the other three quarters were normal in appearance.

INOCULATION EXPERIMENTS WITH FAECES AND MILK.

From the faeces of Cow F, excreted January 29th, 1908, seven guinea-pigs were inoculated intraperitoneally ; of these four died too early for tuberculosis to have developed, and the remaining three, when killed after 33 days, had general tuberculosis.

The milk was collected on each of four days and inoculated into 32 guinea-pigs of which 11 died prematurely. The remaining 21 developed general tuberculosis. Many of the guinea-pigs died in from 18 to 24 days with tuberculosis resembling that following the intraperitoneal inoculation of 0·1 mg. of culture.

2.

COW A.

This animal was a shorthorn heifer in good condition and the diagnosis of tuberculosis depended entirely on the positive result of the tuberculin test.

When killed it was found to have on the right side an enlarged retro-pharyngeal gland which was cystic, with thick fibrous walls and filled with breaking down caseo-necrotic substance. In the Peyer's patches of the small intestine there were three grey nodules containing caseous foci, two soft caseous nodules and a small ulcer in which no tubercle bacilli could be demonstrated. There was also a caseous nodule in a mesenteric gland, caseation of a gluteal gland, and four tubercles in the lungs. All other organs and glands were healthy.

The faeces were collected for 9 days from September 30th, 1907, to October 9th, 1907, and were used to inoculate and feed 41 guinea-pigs of which only one died prematurely.

None of the guinea-pigs developed tuberculosis.

Four young swine were fed for the same length of time with the faecal matter mixed with sterilized milk, the total amount shared between the four from the same trough being 25·6 kilogrammes of faeces. They were tested with tuberculin 59 days after the experiment began and one alone reacted, giving a rise of temperature of 2·6° C. This animal was killed a week later and the post-mortem examination showed tuberculosis of the submaxillary glands on the left side, a caseous focus in one mesenteric gland, four caseating tubercles in the liver and about thirty on the surface beneath the pleura of each lung. The remaining three swine were killed after 90 days and were found to be free from tuberculosis.

COW D.

This animal was fat and in good condition, and the diagnosis of tuberculosis rested entirely upon the positive result of the tuberculin test. At the post-mortem examination the lungs were found to contain discrete tuberculous nodules several of which measured about 10·0 by 6·0 by 5·0 cm. On section, these were composed of softening yellow caseo-necrotic substance surrounded by fibrous walls. A few of the nodules had ulcerated into the bronchi in which soft caseous substance was seen, and muco-pus could be squeezed out of many of the bronchioles. The bronchial and mediastinal glands were enlarged and were to a large extent replaced by bright yellow caseo-necrotic gritty masses.

There was no tuberculosis of any other organ or gland in the body.

Inoculation and Feeding Experiments with Faeces.

The faeces of Cow D were tested on February 20th and 21st and March 24th, 1908, by the inoculation of guinea-pigs and rabbits. Eleven guinea-pigs were inoculated intraperitoneally, of which two became tuberculous; two showed a few tubercles in the omentum containing moderately numerous acid fast bacilli and the remaining seven were free from tuberculosis. Two out of three rabbits inoculated developed tuberculosis. Two swine were fed for 14 days with the faeces and when killed after 79 and 99 days were found to be healthy.

Inoculation and Feeding Experiments with Milk.

The milk was collected by catheter on each of 8 days and was inoculated intraperitoneally into guinea-pigs; in all 60 guinea-pigs were used. None developed tuberculosis.

In several guinea-pigs the omentum contained a few translucent, sometimes whitish, foci, in which a few acid fast bacilli were demonstrated in smear preparations. These bacilli were evidently dead, since guinea-pigs inoculated with the omentums did not develop tuberculosis, and only streptococci were isolated in cultures made from the foci.

COW E.

The condition of this cow was very good: she gave a positive reaction to the tuberculin test. After death there were found in the lungs three small tuberculous nodules and in the caudal mediastinal gland 30 to 40 caseo-calcareous nodules up to a pea in size. In a suprarenal body there was a tubercle the size of a rape-seed in which tubercle bacilli were demonstrated. There was no tuberculosis elsewhere.

Inoculation and Feeding Experiments with Faeces.

From the faeces passed on four days 18 guinea-pigs were inoculated intraperitoneally. Of these five died (three prematurely) and the rest were killed after 50 days. All were free from tuberculosis.

Two swine fed for 14 days with the faeces remained healthy.

Inoculation and Feeding Experiments with Milk.

The milk was collected by catheter on each of six days and 36 guinea-pigs and four rabbits were inoculated intraperitoneally. None developed tuberculosis.

Two swine were fed, each with 650·0 cc., and both remained healthy.

SUMMARY OF RESULTS.

The faeces of five naturally tuberculous cows, out of the total number of six so far investigated, have been found to contain living and virulent tubercle bacilli.

Three of these animals, Cows B, C, and F, were severely diseased and were eliminating large numbers of tubercle bacilli : this is shown by the occurrence of tuberculosis after the inoculation of very small doses of faecal matter in all but one of the guinea-pigs which survived a sufficient length of time, and by the fact that all the swine fed became tuberculous.

Two of the cows, A and D, were in apparently excellent condition of health. One, Cow A, showed after death a caseous and cystic posterior pharyngeal gland, a few small nodules in the intestine, and slight disseminated tuberculosis. The faeces of this animal caused tuberculosis in one out of four swine fed : the other three swine and all the guinea-pigs inoculated remained healthy. The other cow, D, had tuberculosis of the lungs, bronchial and mediastinal glands, without any disease elsewhere. The faeces of this animal caused tuberculosis in three guinea-pigs and two rabbits ; two swine fed remained healthy.

The faeces of the sixth cow, E, which had slight tuberculosis of the lungs and a mediastinal gland, did not give rise to tuberculosis in any of the animals inoculated. Four, Cows A, B, C, and F, out of the five cows which gave positive results showed some tuberculosis of the alimentary tract, but in at least one case, Cow C, it was not sufficient to account for the large numbers of tubercle bacilli in the faeces. These bacilli must have been coughed up from the lungs and swallowed.

Tuberculosis was present in the uterus of each of the severely infected cows and the uterine discharge contained numerous tubercle bacilli. Such a condition constitutes another source of infection.

The milk of two of the cows, B and C, caused, though not invariably, tuberculosis in guinea-pigs inoculated with relatively small doses. The milk was withdrawn from the udder by catheterization, and post-mortem examination of the udders revealed no macroscopic evidence of tuberculosis. Small pieces were examined histologically by Dr. Eastwood and were found to be normal, but it is of course impossible positively to exclude microscopical lesions. The milk of a third cow, F, caused severe tuberculosis in every guinea-pig which lived a sufficient period of time after inoculation. The udder, except for four small nodules in the left hind quarter, was normal to the naked eye : the animal was very ill at the time the milk was collected.

The milk of the remaining two cows, D and E, tested did not give rise to tuberculosis in any of the animals inoculated.

The results of the post-mortem examinations of the naturally infected cows and the details of the inoculation and feeding experiments with guinea-pigs and swine are included in the following pages.

COW B.

PAGE.
Post-mortem notes 16
Post-mortem notes of Calf 16
Guinea-pigs inoculated and fed with Faeces 17
Guinea-pigs inoculated with Milk 18
Post-mortem notes of Swine fed with Faeces 21
Post-mortem notes of Swine fed with Milk 23

COW C.

Post-mortem notes 24
Guinea-pigs inoculated and fed with Faeces 25
Guinea-pigs inoculated with Milk 26
Post-mortem notes of Swine fed with Faeces 27

COW F.

Post-mortem notes 28
Guinea-pigs inoculated and fed with Faeces 29
Guinea-pigs inoculated with Milk 29

COW A.

Post-mortem notes 30
Guinea-pigs inoculated and fed with Faeces 30
Post-mortem notes of Swine fed with Faeces 31

COW D.

Post-mortem notes 33
Guinea-pigs inoculated and fed with Faeces 33
Guinea-pigs inoculated with Milk 34

COW E.

Post-mortem notes 36
Guinea-pigs inoculated and fed with Faeces 36
Guinea-pigs inoculated with Milk 37

Swine fed with the Milk of Cows D and E 38
Swine fed with the Faeces of Cows D and E 38
Control Pigs 38

SHORTHORN COW B.

POST-MORTEM EXAMINATION.

General Condition.—Poor.

Tongue.—Normal.

Tonsils.—The tonsils on both sides were enlarged and firm and were infiltrated with tuberculous tissue, in parts breaking down forming ragged walled cavities.

Pharynx.—Normal.

The Right Submaxillary and Right Superior Cervical Glands.—Each showed an early caseous nodule.

The Left Submaxillary Gland was normal.

The Left Retro-pharyngeal Gland was more than half caseous. The right retro-pharyngeal gland was twice the size of the left and almost caseous throughout.

Cervical Glands.—The left superior cervical, and the middle and lower cervical glands on both sides contained firm caseous nodules, replacing the greater part of the gland substance.

Abdomen.

In the Omentum.—There were a few scattered grey nodules.

On the Peritoneal Surface of the Diaphragm there were loosely attached fibro-caseous nodules occurring singly and in clusters.

Intestines.—In each of the Peyer's patches of the first two-thirds of the small intestine there were from one to eight ulcers varying up to 1·5 cm., they were circular and had slightly raised undermined edges with injected vessels around. In some the floors were clean, in others covered with a little caseous substance; the bases and sides were infiltrated with caseous tubercles. In several places the ulcers coalesced becoming serpiginous. The Peyer's patches in the last third of the small intestine were not affected. Altogether about sixty ulcers were counted and there were also scattered small caseous nodules not yet ulcerated.

Large Intestine.—Normal.

Two Gastric Glands were partly caseous.

Mesenteric Glands.—The mesenteric glands were reatly enlarged and all were replaced by caseo-necrotic tissue which was pinkish in parts and bright yellow in others.

Colic Glands.—Similarly affected.

Spleen.—In the centre of the spleen there was a bright yellow softening caseous gritty nodule 5 mm. in diameter.

Liver.—The surface of the liver showed numerous depressions varying up to 1·0 and 1·5 cm., they were dark red in colour and on section were composed of soft tissue, from which blood welled readily; when all the blood was squeezed out a spongy tissue was left, quite different from the parenchyma. These areas were scattered thoughout the liver substance. No tubercles could be seen on the surface and on section through the substance, one miliary nodule was found.

Portal Glands.—In the portal glands there was an occasional caseous gritty nodule up to a hemp seed in size.

Kidneys.—The cortices of the kidneys were speckled with grey nodules varying up to a millet seed in size. On section they were irregular, many elongated, and the majority showed minute white centres.

Suprarenal Bodies.—In the right suprarenal there was a nodule nearly 1·0 cm. in diameter waxy and caseous with a more opaque yellowish centre.

Left Suprarenal Body.—Normal.

Iliac Glands.—Five iliac glands were greatly enlarged and practically replaced by waxy caseated tissue.

Lumbar Glands.—One lumbar gland contained a caseating nodule; the other glands appeared normal.

Coeliac Glands.—Enlarged and caseous throughout.

Uterus.—The cotyledons of the uterus were large and firm and on section the walls were found to be composed throughout of tuberculous tissue. The internal surfaces were roughened and covered with yellow muco-purulent discharge, such as constantly issued during life from the vagina.

Thorax.

Pleura.—Along the ribs on the parietal pleura there were numerous flattened tuberculous nodules, in places forming thickened areas and in others clusters.

Lungs.—The right anterior lobe was adherent to the pericardium and to the pleura by means of thickened caseous growths. On the surfaces of the lungs there were scattered fibro-caseous nodules and fairly numerous fibrous nodules in the fringes along the margins. About one third of the left caudal lobe and half of the right, at their posterior extremities, were in a condition of caseous pneumonia. On section the masses were soft and caseo-purulent and many had become partly emptied leaving cavities. The rest of the lung tissue was crepitant containing a few pneumonic lobules and was beset with numerous caseating miliary tubercles.

Caudal Mediastinal Gland.—Measured 27·0 by 12·0 cm. and weighed 2lbs. 4ozs. On section it consisted entirely of waxy caseating tissue in which were embedded bright yellow necrotic nodules. The other mediastinal and bronchial glands were enlarged and resembled the caudal mediastinal gland.

Trachea.—Along the whole length of the trachea were numerous small flattened congested tubercles and there was a caseous nodule on the larynx.

Heart.—Normal.

The Right Axillary and Right Gluteal Glands.—Each showed a small caseous nodule.

Parotid, Prescapular, Prepectoral, Left Axilliary, Left Gluteal, Precrural, Popliteal, and Ischiatic Glands.—Normal.

Microscopical Examination.

(Smear preparations.)

Liver (hæmorrhagic area).—No tubercle bacilli.

Kidney (nodule).—No tubercle bacilli.

CALF OF COW B.

POST-MORTEM EXAMINATION.

Condition.—Good.

Abdomen.

Liver.—In the liver just beneath the capsule there were thirteen grey tubercles with minute opaque centres about the size of rape seed. Similar tubercles were seen scattered throughout the substance, one attaining the size of a millet seed; they were grey with yellowish slightly gritty centres.

Portal Glands.—The portal glands were enlarged and on section they showed their cortices fairly closely filled with yellow gritty caseous nodules up to 3 mm. in diameter; in places becoming confluent they formed caseous patches.

Spleen.—In the spleen there were five grey nodules, with a fine yellowish caseous gritty central network, varying up to a wheat grain in size.

Peritoneum and Omentum.—Normal.

Intestines.—Normal.

Mesenteric Glands.—In one mesenteric gland there was a single caseous tubercle.

Kidneys.—Normal.

Suprarenal Bodies.—Normal.

Renal, Coeliac, Lumbar, and Iliac Glands.—Normal.

Thorax.

Pleura.—Normal.

Lungs.—The lungs were crepitant and pink except for some congestion of the dorsal surfaces of the caudal lobes; they showed on the surface a few scattered reddish nodules, some with definite caseous foci.

Mediastinal and Bronchial Glands.—The caudal mediastinal gland showed part of its cortex filled with a coarse yellowish caseous network gritty from calcification, the rest of the gland containing discrete nodules. The other mediastinal and bronchial glands showed discrete yellowish caseous gritty nodules up to 5·0 mm. in diameter.

Heart.—Normal.

Tongue, Larynx, Pharynx, and Tonsils.—Normal.

The Right Precrural Gland showed one yellowish caseous nodule about 2 mm. in diameter

Various Lymphatic Glands.

Parotid, Submaxillary, Cervical, Pharyngeal, Prescapular, Axillary, Left Precrural, Pudic, Popliteal, Gluteal, and Ischiatic Glands.—Normal.

Testes.—Normal.

Microscopical Examinations.

(Smear preparations.)

Liver (nodule).—Three tubercle bacilli seen.

Portal Gland.—Showed a few tubercle bacilli.

Lung (nodule).—One tubercle bacillus seen.

Mesenteric Gland.—Showed a few tubercle bacilli.

GUINEA-PIGS INOCULATED INTRAPERITONEALLY WITH FAECES OF COW B.

Number.	Date of Inoculation.	Dose.	Duration of Life.	Result.
2648	October 1, 1907	2·0 cc.	Died 1 day	Acute infection. No T.
2649		1·5 cc.	Died 1 day	Acute infection. No T.
2650		·5 cc.	Killed 31 days	Early G.T.
2651		1·0 cc.	Died 1 day	Acute infection. No T.
2652		1·0 cc.	Died 2 days	Acute infection. No T.
2669	October 3, 1907	·5 cc.	Died 1 day	Acute infection. No T.
2670		·5 cc.	Died 1 day	Acute infection. No T.
2671		·5 cc.	Killed 28 days	G.T.
2672		·05 cc.	Killed 29 days	Early G.T.
2685	October 4, 1907	·05 cc.	Killed 28 days	Omentum contained 8 nodules and spleen 5. Caseation of portal gland.
2686		·05 cc.	Killed 28 days	A few tubercles in omentum and on peritoneum: opaque foci in spleen and pyloric gland.
2687		·05 cc.	Killed 28 days	Several tubercles in omentum, and caseation of pyloric, portal, and lumbar glands.
2692	October 5, 1907	·05 cc.	Killed 30 days	Early G.T.
2693		·05 cc.	Killed 30 days	Early G.T.
2694		·05 cc.	Died 1 day	Acute infection. No T.
2695		·05 cc.	Killed 30 days	Early G.T.
2710	October 8, 1907	·05 cc.	Killed 27 days	No tuberculosis. ? inoculation intra-caecal.
2711		·05 cc.	Killed 27 days	G.T.
2712		·05 cc.	Killed 27 days	G.T.
2713		·05 cc.	Killed 27 days	G.T.
2720	October 9, 1907	·1 cc.	Died 2 days	Acute infection. No T.
2721		·05 cc.	Killed 27 days	Omentum thickened; pyloric gland caseous.
2722		·05 cc.	Killed 27 days	Similar to above.
2723		·05 cc.	Killed 27 days	Similar plus caseation of lumbar and portal glands.
2724		·05 cc.	Killed 27 days	Early G.T.

GUINEA-PIGS FED WITH FAECES OF COW B.

DOSE IN EACH CASE 1·0 CC. OF FAECAL EMULSION.

Number	Date of Feeding.	Duration of Life.	Result.
2653	October 1, 1907	Killed 98 days	No tuberculosis.
2654		Killed 98 days	No tuberculosis.
2665	October 2, 1907	Killed 98 days	No tuberculosis
2666		Killed 98 days	No tuberculosis.
2673	October 3, 1907	Killed 26 days	No tuberculosis.
2674		Killed 98 days	No tuberculosis.
2688	October 4, 1907	Killed 98 days	No tuberculosis.
2689		Died 81 days	No tuberculosis.
2696	October 5, 1907	Killed 98 days	No tuberculosis.
2697		Killed 98 days	No tuberculosis.
2704	October 7, 1907	Killed 98 days	No tuberculosis.
2705		Killed 98 days	No tuberculosis
2708	October 8, 1907	Killed 98 days	No tuberculosis.
2709		Killed 98 days	No tuberculosis.
2718	October 9, 1907	Killed 98 days	No tuberculosis.
2719		Killed 98 days	No tuberculosis.

GUINEA-PIGS FED CONTINUOUSLY WITH FAECES OF COW B MIXED WITH STERILIZED MILK.

Number.	Date of Feeding.	Duration of Life.	Result.
2642	From October 1, 1907, to October 9, 1907.	Killed 56 days	No tuberculosis.
2643		Killed 97 days	No tuberculosis.
2644		Killed 97 days	No tuberculosis.
2645		Killed 105 days	No tuberculosis.
2646		Killed 105 days	No tuberculosis.
2647		Died 7 days	No tuberculosis.

GUINEA-PIGS INOCULATED INTRAPERITONEALLY WITH THE MILK OF COW B.

Number.	Date of Inoculation.	Dose.	Quarter of Udder.	Duration of Life.	Result.
2734	October 11, 1907	5·0 cc. of milk plus deposit of 20·0 cc. obtained by the centrifuge.	R.F.	Killed 83 days	No tuberculosis.
2735			R.F.	Killed 83 days	No tuberculosis.
2736			R.H.	Killed 83 days	No tuberculosis.
2737			R.H.	Killed 83 days	No tuberculosis.
2738			L.F.	Killed 83 days	No tuberculosis.
2739			L.F.	Killed 83 days	No tuberculosis.
2740			L.H.	Killed 83 days	No tuberculosis.
2741			L.H.	Killed 83 days	No tuberculosis.

GUINEA-PIGS INOCULATED INTRAPERITONEALLY WITH THE MILK OF COW B—*continued.*

Number.	Date of Inoculation.	Dose.	Quarter of Udder.	Duration of Life.	Result.
2742	October 14, 1907	10·0 cc. of milk plus the deposit of 20·0 cc. obtained by the centrifuge.	R.F.	Killed 80 days	No tuberculosis.
2743			R.F.	Killed 80 days	No tuberculosis.
2744			R.H.	Killed 80 days	No tuberculosis.
2745			R.H.	Killed 80 days	No tuberculosis.
2746			L.F.	Killed 80 days	No tuberculosis.
2747			L.F.	Died 74 days	No tuberculosis.
2748			L.H.	Killed 80 days	No tuberculosis.
2749			L.H.	Killed 80 days	No tuberculosis.
2752	October 15, 1907	do.	R.F.	Killed 79 days	No tuberculosis.
2753			R.F.	Killed 79 days	No tuberculosis.
2754			R.H.	Killed 79 days	No tuberculosis.
2755			R.H.	Killed 79 days	No tuberculosis.
2756			L.F.	Killed 79 days	No tuberculosis.
2757			L.F.	Killed 79 days	No tuberculosis.
2758			L.H.	Killed 79 days	No tuberculosis.
2759			L.H.	Killed 79 days	No tuberculosis.
2760	October 16, 1907	do.	R.F.	Killed 79 days	No tuberculosis.
2761			R.F.	Killed 79 days	No tuberculosis.
2762			R.H.	Killed 79 days	No tuberculosis.
2763			R.H.	Killed 79 days	No tuberculosis.
2764			L.F.	Killed 79 days	No tuberculosis.
2765			L.F.	Killed 79 days	G.T. No disease of omentum. ? spontaneous tuberculosis.
2766			L.H.	Killed 79 days	No tuberculosis.
2767			L.H.	Killed 79 days	No tuberculosis.
2768	October 17, 1907	do.	R.F.	Killed 79 days	No tuberculosis.
2769			R.F.	Died 77 days	No tuberculosis.
2770			R.H.	Killed 79 days	No tuberculosis.
2771			R.H.	Killed 79 days	No tuberculosis.
2772			L.F.	Killed 79 days	No tuberculosis.
2773			L.F.	Killed 79 days	No tuberculosis.
2774			L.H.	Killed 79 days	No tuberculosis.
2775			L.H.	Killed 79 days	No tuberculosis.
2776	October 18, 1907	do.	R.F.	Killed 78 days	No tuberculosis.
2777			R.F.	Killed 78 days	No tuberculosis.
2778			R.H.	Killed 78 days	No tuberculosis.
2779			R.H.	Killed 78 days	No tuberculosis.
2780			L.F.	Killed 78 days	No tuberculosis.
2781			L.F.	Killed 78 days	No tuberculosis.
2782			L.H.	Killed 78 days	No tuberculosis.
2783			L.H.	Killed 78 days	No tuberculosis.
2787	October 19, 1907	do.	R.F.	Killed 47 days	No tuberculosis.
2788			R.F.	Died 46 days	G.T. Omentum thickened.
2789			R.H.	Killed 79 days	No tuberculosis.
2790			R.H.	Killed 47 days	No tuberculosis.

GUINEA-PIGS INOCULATED INTRAPERITONEALLY WITH THE MILK OF COW B—*continued.*

Number.	Date of Inoculation.	Dose.	Quarter of Udder.	Duration of Life.	Result.
2791	October 19, 1907	10·0 cc. of milk plus the deposit of 20·0 cc. obtained by the centrifuge.	L.F.	Killed 79 days	No tuberculosis.
2792			L.F.	Killed 47 days	No tuberculosis.
2793			L.H.	Killed 79 days	No tuberculosis.
2794			L.H.	Killed 47 days	No tuberculosis.
MILK WITHDRAWN AFTER THE INOCULATION OF COW WITH TUBERCULIN.					
2882	November 6, 1907	do.	R.F.	Killed 63 days	No tuberculosis.
2883			R.F.	Killed 63 days	No tuberculosis.
2884			R.H.	Died 39 days	G.T. Omentum thickened by fibro-caseous nodules.
2885			R.H.	Killed 63 days	No tuberculosis.
2886			L.F.	Killed 63 days	No tuberculosis.
2887			L.F.	Killed 63 days	G.T.
2888			L.H.	Killed 63 days	G.T.
2889			L.H.	Killed 63 days	G.T.
2890	November 7, 1907	do.	R.F.	Killed 62 days	Early G.T.
2891			R.F.	Killed 62 days	Early G.T.
2892			R.H.	Killed 62 days	No tuberculosis.
2893			R.H.	Died 19 days	A few tubercles in omentum containing tubercle bacilli.
2894			L.F.	Killed 62 days	G.T.
2895			L.F.	Killed 62 days	G.T.
2896			L.H.	Killed 62 days	Caseation of inguinal gland with T.B. No local lesion seen.
2897			L.H.	Killed 62 days	Early G.T.

MILK OF COW B WITHDRAWN IN THE ORDINARY WAY: UDDER CLEANSED.

Number.	Date of Inoculation.	Dose in each case.	—	Duration of Life.	Result.
2874	November 4, 1907	10·0 cc. of milk plus the deposit of 48·0 cc. obtained by the centrifuge.	Mixed milk	Killed 65 days	G.T. severe.
2875				Killed 65 days	G.T. severe.
2876				Killed 65 days	No tuberculosis.
2877				Died 10 days	No tuberculosis.

MILK OF COW B WITHDRAWN IN THE ORDINARY WAY: UDDER UNCLEANSED.

Number.	Date of Inoculation.	Dose in each case.	—	Duration of Life.	Result.
2878	November 5, 1907	10·0 cc. of milk plus the deposit of 48·0 cc. obtained by the centrifuge.	Mixed milk	Killed 64 days	Early G.T.
2879				Killed 64 days	Early G.T.
2880				Killed 64 days	No tuberculosis.
2881				Killed 64 days	No tuberculosis.

PIG 212.

Fed with the faeces of Cow B from October 1, 1907, to October 9, 1907.

Dose—One-fourth part of 19·11 kilogrammes of faeces.

Age—11 weeks.

Killed in good health—January 3, 1908. [94 days after feeding began.]

Weights.

	qrs.	lbs.
October 1, 1907	1	4
January 3, 1908	2	23

Gain in weight.—1 qr. 19 lbs.

Tuberculin Tests.—September 16, 1907. [15 days before the experiment began.] Reaction : Negative. November 28, 1907. [58 days after the experiment began.] Reaction : Positive. Rise of temperature 2·6° Centigrade.

POST-MORTEM EXAMINATION.

General Condition.—Good.

Tongue, Pharynx, and Larynx.—Normal.

Tonsils.—Each tonsil contained two or three firm congested patches up to 1 cm. in area beset with caseous foci.

On the Left Side of the Neck extending from the angle of the jaw to the root of the ear there was a chain of glands, the most anterior of which was the largest and measured 5·0 by 4·0 by 2·5 cm. On section it consisted of firm grey tissue with a close network of yellowish caseated tissue. At one extremity there was a caseous gritty nodule which easily shelled out. The next gland measuring 4·0 by 2·0 cm. was firm and grey with an early caseous network. Of the rest of the glands, one was filled with a caseous network, another contained caseous foci and several small glands were normal. On the right side of the neck the most anterior gland measured 6·0 by 4·0 by 2·5 cm.; on section it consisted of firm grey tissue extensively replaced by a caseous gritty network. Of the other lymphatic glands two were moderately enlarged and closely beset with small caseous patches.

The Left Prescapular Gland showed a minute opaque focus.

The Right Prescapular Gland and Cervical Glands were normal.

Abdomen.

Omentum.—Normal.

Peritoneum.—On the peritoneal surface of the diaphragm on the right side there were some flattened grey nodules where the liver had been in contact with it.

Stomach and Intestines.—Normal.

Mesenteric Glands. — Several of the mesenteric glands were a little enlarged and contained softening caseous nodules which easily shelled out; in the rest of the mesenteric glands there were occasionally found small collections of caseous tubercles.

Spleen.—The spleen contained about a dozen grey nodules, caseous in the centre, varying from a millet seed up to a large pea in size.

Liver.—On the surface of the liver beneath the capsule there were moderately numerous irregular grey nodules, with opaque caseous centres, varying from about 0·5 mm. to 2·0 mm. in diameter, those nearest to the surface had attached to them fibrinous fringes. On section similar nodules were evenly distributed throughout the substance.

Portal Glands.—The portal glands were enlarged and consisted of firm grey tissue beset with caseating streaks and foci.

Kidneys.—Normal.

Suprarenal Bodies.—Normal.

Coeliac Glands.—The coeliac glands were firm and beset with irregular caseous patches and foci.

Lumbar and Iliac Glands.—Normal.

Thorax.

Pleura.—On the pleural surface of the diaphragm there were two loosely attached fibrous growths.

Lungs.—In the lungs were scattered grey translucent nodules, with opaque caseous centres, the majority varying between a rape seed and a hemp seed in size; in the anterior lobes of each lung, however, there were several congested nodules beset with caseous foci up to 6·0 mm. in diameter; the nodules were situated mainly just beneath the pleura.

Dorsal Mediastinal Glands.—Normal.

The Bronchial Glands on each side although very little enlarged were beset with caseous foci.

Inguinal and Precrural Glands normal.

PIG 214.

Fed with the faeces of Cow B from October 1, 1907, to October 9, 1907.

Dose—One-fourth part of 19·11 kilogrammes of faeces.

Age—11 weeks.

Killed in good health—December 3, 1907. [63 days after the experiment began.]

Weights.

	qrs.	lbs.
October 1, 1907	1	8
December 3, 1907	2	0

Gain in weight.—20 lbs.

Tuberculin Tests.—September 16, 1907. [15 days before the experiment began.] No reaction. November 28, 1907. [58 days after the experiment began.] Positive reaction. Rise of temperature 3·0° Centigrade.

POST-MORTEM EXAMINATION.

Carcass in good condition.

Tongue, Larynx, and Pharynx.—Normal.

Right Tonsil.—Normal.

In the Left Tonsil there was an ulcer 5·0 mm. in diameter with thin irregular undermined edges and base covered with a little whitish substance.

On the Left Side of the Neck, four of the glands below and posterior to the angle of the jaw, were enlarged varying in size from a sparrow's egg up to a pheasant's egg. On section they were composed throughout of firm pinkish caseo-necrotic tissue with fine yellowish gritty streaks. Three small glands were not affected.

Cervical Glands.—The left cervical glands were slightly enlarged and showed discrete irregular caseous tubercles.

The right cervical glands were normal.

Prescapular Glands.—The left prescapular gland was about twice the normal and was firm, grey and beset with irregular caseous tubercles.

The right prescapular gland was normal.

Abdomen.

Peritoneum and Omentum.—Normal.

Intestines.—Normal.

Mesenteric Glands.—The mesenteric glands were not obviously enlarged. One gland in the centre had part of its substance a little prominent and firm, showing early caseous patches in the cortex.

Colic Glands.—Normal.

Spleen.—In the spleen there were two caseating nodules the size of hemp seeds and three minute opaque tubercles.

Liver.—On the convex surface of the liver there were ten tubercles and six on the concave, varying in size up to a millet seed. On section they consisted of grey translucent tissue with caseous centres. Similar tubercles were sparsely scattered throughout the substance.

Portal Glands.—In the cortices of the portal glands there were scattered irregular early caseous patches.

Kidneys.—One kidney showed a few minute grey points. The other was normal.

Suprarenal Bodies.—Normal.

Coeliac, Lumbar, and Iliac Glands.—Normal.

Thorax.

Lungs.—The lungs were pink and crepitant. In the anterior and middle lobes of the right there were 18 nodules varying from a rape seed up to 5·0 mm. in diameter. On section they consisted of grey tissue caseated in the centre. There were similar nodules scattered throughout the left anterior and the caudal lobes, one of which attained the size of a pea.

Bronchial Glands.—They were beset with small discrete early caseous patches.

Inguinal and Precrural Glands.—Normal.

Testes.—Normal.

Microscopical Examination.

(Smear preparation.)

Left Tonsil.—No tubercle bacilli. Moderately numerous blue stained organisms.

PIG 216.

Fed with the faeces of Cow B from October 1, 1907, to October 9, 1907.

Dose—One-fourth part of 19·11 kilogrammes of faeces.

Age—11 weeks.

Killed in good health—January 9, 1908. [100 days after feeding began.]

Weights.

	qrs.	lbs.
October 1, 1907	1	8
January 9, 1908	3	7

Gain in weight.—1 qr. 27 lbs.

Tuberculin Tests.—September 16, 1907. [15 days before the experiment began.] Reaction: Negative.

November 28, 1907. [58 days after the experiment began.] Reaction: Positive. Rise of temperature 2·1° Centigrade.

POST-MORTEM EXAMINATION.

General Condition.—Good.

Tongue.—Normal.

Tonsils.—Normal.

Pharynx.—Normal.

Submaxillary Glands.—On the left side of the neck beneath the jaw, the gland situated most anteriorly was the size of a pigeon's egg, and on section was about three quarters replaced by caseous gritty tissue. All the other glands about the jaw on each side of the neck were normal.

Pharyngeal, Cervical, and Prescapular Glands.—Normal.

Abdomen.

Peritoneum.—Normal.

Omentum.—In the omentum there were about four dozen discrete spherical nodules from a rape seed up to 4·0 mm. in diameter. On section they were translucent with yellow caseous centres.

Stomach.—Normal.

Intestines.—Normal.

Mesenteric Glands.—Several of the mesenteric glands at each extremity and three glands in the middle of the mesentery were enlarged and the cortices extensively replaced by yellowish caseous substance, just perceptibly gritty. One gland at one extremity measured 3·0 by 1·5 cm. and was entirely replaced by a pinkish yellow caseo-necrotic substance. Many glands appeared normal; the remainder showing discrete yellow nodules and foci.

Ileo-Colic Glands.—The ileo-colic glands were extensively affected containing numerous yellow caseous nodules.

Colic Glands. — Several showed foci and small nodules.

Spleen.—The spleen showed a dozen nodules up to 5·0 mm. in diameter, two of them being on the surface; the rest could be seen beneath the capsule slightly projecting from the surface. All of them were grey and translucent with irregular yellow caseous centres.

Liver.—There could be seen just beneath the surface of the liver about two hundred and seventy nodules ranging from a point up to 5·0 mm. in diameter; the smallest were grey and translucent throughout, the larger ones were grey with caseous centres or beset with caseous foci. On section the substance contained numerous similar nodules chiefly about 2·5 mm. in diameter.

Portal Glands.—The portal glands were enlarged and they showed their cortices closely beset with large irregular yellow caseous nodules.

Kidneys.—Normal.

Suprarenal Bodies.—Normal.

The Renal and Lumbar Glands were enlarged (the largest and most severely affected being on the left side of the spine), and showed numerous irregular yellow caseous foci, which in places had run together forming large nodules with a caseous network, just perceptibly gritty.

Iliac Glands.—Two left iliac glands showed a few minute caseous foci.

Right Iliac Glands.—Normal.

Coeliac Glands.—(Seven in number), four were enlarged and showed fairly numerous yellow irregular caseous nodules up to 3 and 4 mm. in diameter ; the rest appeared normal.

Thorax.

Diaphragm. — On the peritoneal surface of the central tendon of the diaphragm, mainly on the right side, there were two dozen nodules up to about 6·0 mm. in diameter, many of which extended through the diaphragm and formed nodules on the pleural surface ; they were grey and translucent and beset with yellow caseous foci. There were two similar nodules on the right pleura.

Lungs.—The lungs were pink and crepitant, they showed on the surface about one hundred and fifty nodules up to 5·0 and 6·0 mm. in diameter; the smallest were grey with opaque centres : the largest were considerably caseated and gritty. In each of the anterior and middle lobes there was a single nodule, from 0·8 to 1·0 cm. in diameter, they were grey and translucent with a fine caseous network. On section the lung parenchyma showed moderately numerous similar nodules.

Thoracic Lymphatic Glands.

The Bronchial and Mediastinal Glands were enlarged and showed their cortices closely beset with yellow caseating nodules in places forming a coarse network.

Pericardium.—Normal.

Heart.—Normal.

Inguinal Glands.—One on the left side contained a small irregular yellow caseous nodule ; other inguinal and precrural glands normal.

PIG 218.

Fed with the faeces of Cow B from October 1, 1907, to October 9, 1907.

Dose—One-fourth part of 19·11 kilogrammes of faeces.

Age—11 weeks.

Killed in good health—December 11, 1907. [71 days after the experiment began.]

Weights.

	qrs.	lbs.
October 1, 1907...	1	7
December 11, 1907	2	7

Gain in weight.—1 qr. 0 lbs.

Tuberculin Tests.—September 16, 1907. [15 days before the experiment began.] No reaction.

November 28, 1907. [58 days after the experiment began.] Positive reaction. Rise of temperature 1·3° Centigrade.

POST-MORTEM EXAMINATION.

Carcass in good condition.

Tongue, Tonsils, Larynx, and Pharynx.—Normal.

On the Right Side beneath the Jaw anterior to the submaxillary salivary gland there was a gland measuring 3·3 by 2·5 by 1·3 cm. On section the substance was firm, translucent and more than half replaced by a pinkish caseous gritty nodule and with discrete tubercles in the remaining part.

A second smaller gland contained a caseous network.

The glands posterior to the salivary gland were normal.

Left Submaxillary Gland.—Normal.

Cervical and Prescapular Glands.—Normal.

Abdomen.

Stomach.—Normal.

Intestines.—Normal.

Omentum.—Normal.

Peritoneum.—Normal.

Mesenteric Glands.—In one mesenteric gland there was a caseating nodule 3·0 mm. in diameter, there was a slightly larger irregular nodule in a second. A third gland showed part of its substance replaced by a caseous network and a fourth gland was slightly enlarged at one extremity and contained an irregular waxy caseating nodule 1·0 cm. in diameter.

Spleen.—Normal.

Liver.—On the surface beneath the capsule of the liver there were eight grey tubercles with opaque centres up to a rape seed in size. On section through the substance an occasional grey tubercle was seen.

Portal Glands.—In the portal glands there were a few caseous foci.

Kidneys.—Normal.

Suprarenal Bodies.—Normal.

Renal, Coeliac, Lumbar and Iliac Glands.—Normal.

Thorax.

Lungs.—The left lung showed on the surface beneath the pleura, two grey submiliary tubercles with opaque centres. In the right there were three similar tubercles.

Bronchial Glands.—There was a caseous focus in a left bronchial gland. The right bronchial gland was normal.

Mediastinal Glands.—Normal.

Inguinal and Precrural Glands.—Normal.

PIG 222.

Fed once with the milk from Cow B.

Date—November 1, 1907.

Dose—2,870 cubic centimetres.

Age—11 weeks.

Killed in good health—January 9, 1908. [69 days after the experiment began.]

Weights.

	qrs.	lbs.
November 1, 1907	1	14
January 9, 1908	2	26

Gain in weight.—1 qr. 12 lbs.

Tuberculin Tests.—October 11, 1907. [20 days before the experiment began.] No reaction.

November 28, 1907. [27 days after the experiment began.] No reaction.

POST-MORTEM EXAMINATION.

General Condition.—Good.

There was no sign of tuberculosis.

PIG 224.

Fed with the milk of Cow B from October 14, 1907, to October 20, 1907.

Dose one-half part of 18,490 cubic centimetres.

Age—9 weeks.

Killed in good health—January 8, 1908. [86 days after the experiment began.]

Weights.

	qrs.	lbs.
October 14, 1907	1	0
January 8, 1908	2	6

Gain in weight.—1 qr. 6 lbs.

Tuberculin Tests.—October 11, 1907. [3 days before experiment began.] Reaction : Negative.

November 28, 1907. [45 days after the experiment began.] Reaction : Negative.

POST-MORTEM EXAMINATION.

General Condition.—Good.

There was no sign of tuberculosis.

PIG 226.

Fed with the milk of Cow B from October 14, 1907, to October 20, 1907.

Dose—One-half part of 18,490 cubic centimetres.

Age—9 weeks.

Killed in good health—January 8, 1908. [86 days after the experiment began.]

Weights.

	qrs.	lbs.
October 14, 1907	1	5
January 8, 1908	2	0

Gain in weight.—23 lbs.

Tuberculin Tests.—October 11, 1907. [3 days before the experiment began.] No reaction.

November 28, 1907. [45 days after the experiment began.] No reaction.

POST-MORTEM EXAMINATION

General Condition.—Good.

There was no sign of tuberculosis.

JERSEY COW C.

POST-MORTEM EXAMINATION.

Body emaciated.

Thorax.

Pleura.—On the pleura along the ribs there were numerous flattened fibro-caseous nodules up to 2·0 cm., some loosely attached. There were numerous similar nodules on the pleura over the dorsal mediastinal glands. On the pleural surface of diaphragm there were a few small loosely attached fibro-caseous nodules.

Lungs.—The lungs were very heavy and voluminous. On the pleural surfaces there were numerous flattened perlsucht growths similar to but larger than those on the parietal pleura varying up to 4·0 cm. in diameter. In both anterior lobes there were large caseo-necrotic masses replacing a third of the substance, the rest of the anterior lobes was closely beset with nodules and masses varying in size. The posterior lobes were similarly severely affected. On section the masses were bright yellow, caseo-necrotic and in many parts becoming soft and caseo-purulent around the margins. The bronchi were filled with muco-pus and in several places caseous substance could be seen protruding into the cavity of a bronchus.

There was a cast of the trachea formed of inspissated muco-pus.

Mediastinal Glands.—The long mediastinal gland weighed 2 lbs. and measured 26·0 by 10·0 by 6·0 cm. On section it consisted almost throughout of bright yellow caseo-necrotic substance.

Bronchial Glands.—The bronchial glands were similarly greatly enlarged and caseo-necrotic throughout.

Other mediastinal and supra-bronchial glands were similar.

Heart and Great vessels.—Normal.

Abdomen.

Omentum and Peritoneum.—Normal.

Intestines.—All the Peyer's patches of the small intestine contained a few caseous nodules varying from a millet seed up to a hemp seed, many of them ulcerated on the surface. In addition there were several small ulcers 5·0 mm. in diameter from which the caseous substance had almost disappeared.

Mesenteric Glands.—The majority of the mesenteric glands appeared normal; several contained discrete caseous nodules and a few at one extremity showed the cortices diffusely caseous. One mesenteric gland about the centre of the mesentery was greatly enlarged measuring 8·0 by 4·0 by 5·5 cm., on section it consisted practically throughout of an orange yellow caseo-necrotic slightly gritty substance.

Spleen.—Weighed 1 lb. 6 ozs. On section it contained ten caseous gritty tubercles varying from a rape seed up to a millet seed in size.

Liver.—Anterior surface normal. On the postero-inferior surface there was a single caseous tubercle. On section through the substance three caseous foci were met with, of which one was gritty.

Gall Bladder.—Normal.

Portal Glands.—The portal glands contained a few discrete caseous nodules, the size of hemp seed.

Kidneys.—Both kidneys showed in the cortices just beneath the surface scattered tubercles varying from a rape seed up to a hemp seed in size; they were all caseous and the largest slightly gritty. On section similar nodules were found scattered throughout the deeper parts of the cortices.

Suprarenal Bodies.—The left suprarenal body contained ten, and the right five, caseo-calcareous nodules from a rape seed up to 3·5 mm. in diameter.

Lumbar and Iliac Glands.—Normal.

Tongue, Tonsils, Larynx, Pharynx, and Trachea.—Normal.

Uterus.—The walls of both cornua of the uterus and also the common portion were thickened and infiltrated with a network of grey nodules with bright yellow caseous centres. The cavity was filled with purulent fluid and caseous flocculi.

Supramammary Glands. — Each supramammary gland showed a minute caseous focus ; one contained also a grey nodule the size of a hemp seed, diffusely caseous.

The Udder.—Normal.

Retro-Pharyngeal Glands.—The left was congested and showed a number of caseo-calcareous masses arranged around the cortex. The right contained two caseous miliary tubercles.

Cervical Glands.—The right inferior cervical gland was enlarged and about three-quarters of the cortex was replaced by yellow caseo-calcareous masses ; other cervical glands were normal.

Parotid, Prepectoral, Prescapular, Precrural, Axillary, Popliteal, and Gluteal Glands.—Normal.

Microscopical Examination.

(Smear preparations.)

Supramammary Gland (focus).—(1) Three tubercle bacilli.

Supramammary Gland (focus).—(2) Two tubercle bacilli.

Intestine (ulcer).—A moderate number of tubercle bacilli.

Bronchial Gland.—No tubercle bacilli.

GUINEA-PIGS INOCULATED WITH THE FAECES OF COW C.

Number.	Date of Inoculation.	Dose.	Method of Inoculation.	Duration of Life.	Result.
2805	October 24, 1907	·05 cc.	Ip.	Killed 22 days	G.T.
2806		·1 cc.	Ip.	Killed 18 days	G.T.
2807		·1 cc.	Sub.	Killed 16 days	No tuberculosis ; discharging ulcers in the skin.
2808		·05 cc.	Ip.	Died 4 days	No tuberculosis.
2809		·05 cc.	Sub.	Killed 32 days	Early G.T.
2810		·05 cc.	Sub. & Ip.	Killed 32 days	G.T. severe.
2813	October 25, 1907	·05 cc.	Ip.	Killed 21 days	G.T.
2814		·1 cc.	Ip.	Killed 20 days	G.T. severe.
2815		·2 cc.	Ip.	Killed 17 days	Single nodule in omentum ; two nodules in spleen ; portal gland caseous.
2816		·1 cc.	Sub.	Killed 34 days	G.T. severe.
2817		·1 cc.	Sub.	Killed 34 days	G.T.
2818		·2 cc.	Sub.	Killed 20 days	No tuberculosis ; ulcer in skin ; no T.B.
2829	October 28, 1907	1·0 cc.	Sub.	Killed 17 days	No tuberculosis. Large ulcer in skin.
2830		·3 cc.	Ip.	Killed 29 days	G.T. severe.
2831		·1 cc.	Sub.	Killed 66 days	G.T. severe.
2832		·2 cc.	Sub.	Died 66 days	G.T. severe.
2833		·2 cc.	Ip.	Died 1 day	Acute infection. No T.
2834		·1 cc.	Ip.	Killed 18 days	Early G.T.
2837	October 29, 1907	·1 cc.	Ip.	Killed 28 days	G.T.
2838		·2 cc.	Ip.	Killed 28 days	G.T.
2839		·3 cc.	Ip.	Died 1 day	Acute infection. No. T.
2840		·1 cc.	Sub.	Killed 30 days	G.T.
2841		·3 cc.	Sub.	Died 3 days	No tuberculosis.
2842		1·0 cc.	Sub.	Died 2 days	No tuberculosis.
2853	October 30, 1907	·2 cc.	Ip.	Died 1 day	Acute infection. No T.
2854		·2 cc.	Ip.	Died 1 day	Acute infection. No. T.
2855		·2 cc.	Ip.	Killed 27 days	G.T.
2856		1·0 cc.	Sub.	Died 5 days	No tuberculosis.
2857		1·0 cc.	Sub.	Died 2 days	No tuberculosis.
2858		1·0 cc.	Sub.	Died 2 days	No tuberculosis.

Ip. = intraperitoneal. Sub. = subcutaneous.

GUINEA-PIGS INOCULATED WITH FAECES OF COW C.

DILUTED WITH SALT SOLUTION ; 1 GRAMME OF FAECES IN 2,000 CUBIC CENTIMETRES OF STERILE SALT SOLUTION.

Number.	Date of Inoculation.	Dose.	Method of Inoculation.	Duration of Life.	Result.
2872	October 31, 1907	1·0 cc.	Ip.	Died 63 days	Severe G.T.
2873		2·0 cc.	Ip.	Killed 63 days	Severe G.T.

GUINEA-PIGS FED WITH FAECES OF COW C.

DOSE IN EACH CASE 1·0 CC. OF FAECAL EMULSION.

Number.	Date of Feeding.	Duration of Life.	Result.
2803	October 24, 1907	Killed 90 days	No tuberculosis.
2804			
2811	October 25, 1907	Killed 89 days	No tuberculosis.
2812			
2827	October 28, 1907	Died 44 days	No tuberculosis.
2828		Killed 86 days	No tuberculosis.
2835	October 29, 1907	Killed 85 days	No tuberculosis.
2836			
2851	October 30, 1907	Killed 84 days	No tuberculosis.
2852			

GUINEA-PIGS FED CONTINUOUSLY WITH FAECES OF COW C MIXED WITH STERILIZED MILK.

Number.	Date of Feeding.	Duration of Life.	Result.
2799	From October 24, 1907, to October 30, 1907.	Killed 74 days	No tuberculosis.
2800		Killed 90 days	Caseous ulcers in intestine, and caseation of mesenteric glands. G.T.
2801		Died 48 days	No tuberculosis.
2802		Killed 90 days	No tuberculosis.

ANIMALS INOCULATED INTRAPERITONEALLY WITH THE MILK OF COW C.

Number of Animal.	Date of Inoculation.	Dose.	Quarter of Udder.	Duration of Life.	Result.
Rabbit 1524	October 25, 1907.	30·0 cc.	R.F.	Died 13 days	No tuberculosis.
Rabbit 1525			R.H.	Killed 76 days	No tuberculosis.
Rabbit 1526			L.F.	Died 18 days	No tuberculosis.
Rabbit 1527			L.H.	Killed 76 days	No tuberculosis.
Guineapig 2819	October 25, 1907.	10·0 cc. of milk plus the deposit of 40·0 cc. obtained by centrifuging.	R.F.	Died 50 days	No tuberculosis.
Guineapig 2820			R.F.	Killed 73 days	No tuberculosis.
Guineapig 2821			R.H.	Killed 73 days	No tuberculosis.
Guineapig 2822			R.H.	Killed 73 days	No tuberculosis.
Guineapig 2823			L.F.	Killed 73 days	No tuberculosis.
Guineapig 2824			L.F.	Killed 73 days	No tuberculosis.
Guineapig 2825			L.H.	Killed 73 days	No tuberculosis.
Guineapig 2826			L.H.	Died 63 days	No tuberculosis.

ANIMALS INOCULATED INTRAPERITONEALLY WITH THE MILK OF COW C—*continued.*

Number of Animal.	Date of Inoculation.	Dose.	Quarter of Udder.	Duration of Life.	Result.
Rabbit 1531	October 29, 1907.	50·0 cc.	R.F.	Killed 72 days	No tuberculosis.
Rabbit 1532			L.F.	Died 3 days	No tuberculosis.
Rabbit 1533			L.H.	Killed 72 days	No tuberculosis.
Guineapig 2843	October 29, 1907	As on Oct. 25.	R.F.	Died 48 days	Three transparent tubercles in omentum containing tubercle bacilli.
Guineapig 2844			R.F.	Killed 71 days	No tuberculosis.
Guineapig 2845			R.H.	Killed 69 days	No tuberculosis.
Guineapig 2846			R.H.	Killed 71 days	No tuberculosis.
Guineapig 2847			L.F.	Died 24 days	Three transparent tubercles in omentum containing moderately numerous tubercle bacilli.
Guineapig 2848			L.F.	Killed 71 days	No tuberculosis.
Guineapig 2849			L.H.	Killed 69 days	No tuberculosis.
Guineapig 2850			L.H.	Killed 71 days	No tuberculosis.
Rabbit 1534	October 30, 1907.	30·0 cc.	R.F.	Died 25 days	Six transparent tubercles in omentum containing moderately numerous T.B.
Rabbit 1535			R.H.	Died 27 days	Several tubercles in omentum, one caseating, containing T.B.
Rabbit 1536			L.F.	Killed 71 days	No tuberculosis.
Rabbit 1537			L.H.	Killed 71 days	Three miliary tubercles and one caseating nodule (6·0 mm.) in omentum. Caseation of portal glands. Four caseating nodules in the lungs.
Guineapig 2859	October 30, 1907.	As on Oct. 25.	R.F.	Killed 71 days	G.T. Omentum contained about fifty nodules.
Guineapig 2860			R.F.	Killed 71 days	Severe G.T.
Guineapig 2861			R.H.	Killed 68 days	Early G.T.
Guineapig 2862			R.H.	Killed 71 days	Severe G.T.
Guineapig 2863			L.F.	Killed 68 days	No tuberculosis.
Guineapig 2864			L.F.	Killed 71 days	No tuberculosis.
Guineapig 2865			L.H.	Killed 68 days	No tuberculosis.
Guineapig 2866			L.H.	Killed 71 days	No tuberculosis.

PIG 230.

Fed with the faeces of Cow C from October 23, 1907, to October 30, 1907.

Dose—5·56 kilogrammes of faeces.

Age—10 weeks.

Killed when in good health—December 11, 1907. [48 days after the experiment began.]

Weights.

	qrs.	lbs.
October 23, 1907	1	11
December 11, 1907	2	7

Gain in weight.—24 lbs.

Tuberculin Tests. — October 11, 1907. [12 days before the experiment began.] No reaction.

November 28, 1907. [36 days after the experiment began.] Positive reaction. Rise of temperature 1·5° Centigrade.

POST-MORTEM EXAMINATION.

General Condition.—Good.

Tongue, Pharynx, and Larynx.—Normal.

Tonsils.—In the tonsils there were a few soft yellowish foci.

On the Left Side of the Neck, beneath the angle of the jaw, anterior to the submaxillary salivary gland, there was a gland measuring 5·0 by 3·0 by 2·2 cm. On section it was composed of firm translucent tissue with a close yellowish network; attached to it was a small gland containing a few opaque foci.

Four glands posterior to the first were normal.

On the Right Side of the Neck, in front of the submaxillary salivary gland, there were two glands forming a mass 5·0 by 3·3 by 2·0 cm. On section it resembled that on the opposite side; the other glands about the jaw were normal.

Cervical Glands.—Normal.

Prescapular Glands.—Normal.

Abdomen.

Stomach.—Normal.

Intestines.—Normal.

Mesenteric Glands.—The majority of the mesenteric glands were normal. About six glands on each side of the mesentery in the centre were moderately enlarged, consisting of firm translucent tissue with a firm yellowish waxy caseous network.

Spleen.—Normal.

Liver.—On the convex surface of the liver there were visible beneath the capsule twenty slightly irregular grey caseating tubercles the size of rape seeds; they were sparsely scattered on the other surfaces and in the substance.

Portal Glands.—One portal gland was a little firm at one extremity and showed early caseous patches. A second small gland was similar.

Kidneys.—Normal.

Suprarenal Bodies.—Normal.

Coeliac, Lumbar, and Iliac Lymphatic Glands.—Normal.

Thorax.

Lungs.—In the left lung on the surface beneath the pleura there were fourteen grey caseating tubercles up to a millet seed in size. The right lung showed rather fewer. On section no more could be seen.

Bronchial Glands.—Normal.

Precrural and Inguinal Glands.—Normal.

Microscopical Examination.

(Smear preparation.)

Tonsil (focus).—Four tubercle bacilli seen.

COW F.

POST-MORTEM EXAMINATION.

General Condition.—Poor.

Tongue.—Normal.

Tonsils.—The tonsils were firm and on section contained caseous nodules.

Submaxillary Glands.—Normal.

Pharyngeal Glands.—The left posterior pharyngeal gland measured 9·5 by 5·5 by 3·0 cm. and on section was caseous throughout.

The right posterior pharyngeal gland measured 7 by 3·5 cm. On section the superficial part of the cortex was caseous.

Cervical Glands.—Several of the cervical glands contained large nodules, some caseous throughout.

Abdomen.

Intestines. — In the small intestine there were counted nineteen ulcers, varying up to 4·0 cm. in diameter; the bases and the raised margins were firm and caseating. There were also scattered nodules in both intestines.

Mesenteric Glands.—The mesenteric glands were enormously enlarged and roplaced by a brownish yellow necrotic substance, in many parts softening. In points of size and appearance the lesions were older than those in the bronchial glands; also the tuberculosis of the lungs was fairly acute.

Spleen.—The spleen appeared normal.

Liver.—On the surface of the liver there was a single small tubercle; the parenchyma was beset throughout with small ill-defined yellowish grey necrotic patches.

Portal Glands.—The cortices of the portal glands were a little firm, but showed no caseation.

Kidneys.—In the medulla of the right kidney there were two caseating miliary tubercles. Left kidney normal.

Suprarenal Bodies. — The left suprarenal body contained three caseous nodules up to a pea in size.

Right suprarenal body showed three similar nodules up to the size of a millet seed.

There was an opaque focus in one renal lymphatic gland.

Lumbar Glands.—Five lumbar glands, up to a pigeon's egg in size, caseous throughout.

Iliac Glands.—Caseo-calcareons nodules in two iliac glands.

Thorax.

Lungs.—The lungs were voluminous, the anterior lobes were congested. The substance was closely beset throughout with irregular and for the most part small caseous nodules and patches. On the left lung there was a number of perlsucht nodules and also numerous similar nodules and masses on the parietal pleura.

Prescapular Glands were not tuberculous. The right gland was enlarged from the tuberculin inoculation.

Prepectoral and Axillary Glands.—Normal.

Supramammary Lymphatic Glands.—Both supramammary glands were enlarged and contained dirty yellow caseo-necrotic masses.

Udder.—In the tissue of the udder of the left hind quarter forming the wall of the main sinus close to the teat, there were four firm reddish grey nodules varying from a millet seed up to a pea; they resembled the tissue around, being distinguished by a central caseous streak and firmness from the tissue in that part of the udder which is mainly composed of ducts. The other quarters of the udder were normal.

Uterus.—In the horns of the uterus there were rounded yellow caseo-necrotic nodules, not unlike unopened mushrooms, projecting into the cavities and loosely attached by pedicles, composed of reddish grey tissue of which the centres of the nodules were also formed; the largest was the size of a robin's egg. There was a muco-purulent exudation in the uterus and vagina.

Microscopical Examination.

(Smear preparations.)

Udder (nodule I and II).—Showed moderately numerous tubercle bacilli.

GUINEA-PIGS WITH FAECES OF COW F.

ALL INTRAPERITONEAL.

Number.	Date of Inoculation.	Dose.	Duration of Life.	Result.
2979	January 29, 1908	1·0 cc.	Died 1 day	Acute infection.
2980		1·0 cc.	Died 1 day	Acute infection.
2981		·5 cc.	Died 11 days	Sub-acute infection.
2982		·5 cc.	Killed 33 days	General tuberculosis.
2983		·5 cc.	Died 8 days	No tuberculosis.
2984		·5 cc.	Killed 33 days	General tuberculosis.
2985		·5 cc.	Killed 33 days	General tuberculosis.

GUINEA-PIGS INOCULATED INTRAPERITONEALLY WITH THE MILK OF COW F.

Number.	Date of Inoculation.	Dose.	Quarter of Udder.	Duration of Life.	Result.
2971	January 29, 1908	6·0 cc. of milk plus the deposit of 24·0 cc. obtained by the centrifuge.	R.F.	Died 35 days	Caseo-purulent nodule in muscle at site of inoculation ; caseation of sternal gland. Numerous T.B. in both.
2972			R.F.	Died 11 days	No tuberculosis.
2973			R.H.	Died 18 days	General tuberculosis.
2974			R.H.	Died 24 days	General tuberculosis.
2975			L.F.	Died 27 days	General tuberculosis.
2976			L.F.	Died 35 days	General tuberculosis.
2977			L.H.	Died 18 days	General tuberculosis.
2978			L.H.	Died 18 days	General tuberculosis.
2986	January 30, 1908	5·0 cc. plus the deposit of 10 cc.	R.F.	Killed 34 days	General tuberculosis.
2987			R.F.	Killed 34 days	General tuberculosis.
2988		As in the first series.	R.H.	Died 17 days	General tuberculosis.
2989			R.H.	Died 7 days	No tuberculosis.
2990			L.F.	Died 10 days	No tuberculosis.
2991			L.F.	Killed 34 days	General tuberculosis.
2992			L.H.	Died 17 days	General tuberculosis.
2993			L H.	Died 4 days	No tuberculosis.
2994	January 31, 1908	7·0 cc.	R.F.	Killed 33 days	General tuberculosis.
2995		7·0 cc.	R.F.	Killed 33 days	General tuberculosis.
2996		As in the first series.	R.H.	Died 23 days	General tuberculosis.
2997			R.H.	Died 9 days	One minute tubercle in omentum. Tubercle bacilli found.
2998			L.F.	Died 6 days	No tuberculosis.
2999			L.F.	Killed 33 days	General tuberculosis.
3000			L.H.	Died 18 days	General tuberculosis.
3001			L.H.	Died 8 days	No tuberculosis.
3002	February 1, 1908	4·0 cc.	R.F.	Killed 32 days	General tuberculosis.
3003		10·0 cc.	R.H.	Died 8 days	No tuberculosis.
3004			R.H.	Died 7 days	No tuberculosis.
3005			L.F.	Killed 32 days	General tuberculosis.
3006			L.F.	Died 8 days	No tuberculosis.
3007			L.H.	Died 3 days	No tuberculosis.
3008			L.H.	Died 22 days	General tuberculosis.

SHORTHORN HEIFER A.

POST-MORTEM EXAMINATION.

General Condition.—Good.

Tongue.—Normal.

Tonsils.—Normal.

Pharynx.—Normal.

Submaxillary Glands.—Normal.

Pharyngeal Glands.—The right retro-pharyngeal gland measured 10·5 by 6·5 by 5·0 cm. On section it was a cyst with thick fibrous walls, filled with caseo-necrotic substance which was partly broken down into a brownish yellow purulent fluid with caseous flakes and partly adherent as congested caseo-necrotic masses to the internal walls.

The left retro-pharyngeal gland measured 4·1 by 3·0 by 1·5 cm. On section it was normal.

Cervical Glands.—Normal.

Abdomen.

Peritoneum and Omentum.—Normal.

Intestines.—In the Peyer's patches of the small intestine there were five nodules, two grey with opaque foci, and three soft yellow and caseous, varying up to about a millet seed in size.

There was also a small ulcer with a fibrous slightly opaque thickened base in which no tubercle bacilli could be demonstrated microscropically.

Large Intestine.—Normal.

Mesenteric Glands.—One mesenteric gland showed a yellow caseo-calcareous nodule nearly 1·0 cm. in diameter.

Spleen.—Normal.

Liver.—Normal.

Portal Glands.—Normal.

Kidneys.—Normal.

Suprarenal Bodies.—Normal.

Renal, Coeliac, Lumbar, and Iliac Lymphatic Glands.—Normal.

Thorax.

Pleura.—Normal.

Lungs.—In the lungs just beneath the pleura there were three translucent foci and a soft grey nodule the size of a hemp seed.

Bronchial and Mediastinal Glands.—Normal.

Heart and Pericardium.—Normal.

Gluteal Glands.—The right was larger than the left, measuring 2·5 by 2·0 cm. On section the substance was firm and infiltrated almost throughout, with a bright yellow caseo-necrotic network mottled with patches of hæmorrhage. The left gluteal gland was normal.

Various Lymphatic Glands.

Parotid, Prescapular, Prepectoral, Precrural, and Popliteal Glands.—Normal.

Udder.—Normal.

Supramammary Glands.—Normal.

Microscopical Examinations.

(Smear preparations.)

Intestine (grey nodule).—One tubercle bacillus.

Intestine (caseous nodule).—No tubercle bacilli.

Intestine (ulcer).—No tubercle bacilli.

Retro-pharyngeal Gland.—Four tubercle bacilli, also short blue stained bacilli.

Lung (grey nodule).—No tubercle bacilli.

Gluteal Gland.—No tubercle bacilli.

GUINEA-PIGS INOCULATED INTRAPERITONEALLY WITH FAECES OF COW A.

Number.	Date of Inoculation.	Dose.	Duration of Life.	Result.
2635	September 30, 1907	Small doses varying up to 0·1 cc.	Killed 92 days	No tuberculosis.
2636			Killed 92 days	No tuberculosis.
2637			Killed 92 days	No tuberculosis.
2638			Killed 56 days	No tuberculosis
2639			Killed 42 days	No tuberculosis.
2659	October 2, 1907	·05 cc.	Killed 30 days	No tuberculosis.
2660		·05 cc.	Killed 40 days	No tuberculosis.
2661		·05 cc.	Killed 55 days	No tuberculosis.
2662		·05 cc.	Killed 36 days	No tuberculosis.
2681	October 4, 1907	·05 cc.	Killed 88 days	No tuberculosis.
2682		·05 cc.	Killed 88 days	No tuberculosis.
2683		·5 cc.	Killed 88 days	No tuberculosis.
2684		·5 cc.	Killed 38 days	No tuberculosis.
2700	October 7, 1907	·05 cc	Killed 85 days	No tuberculosis.
2701		·05 cc	Killed 85 days	No tuberculosis.
2702		·05 cc.	Killed 85 days	No tuberculosis.
2703		·05 cc.	Killed 85 days	No tuberculosis.

GUINEA-PIGS FED WITH FAECES OF COW A.

Dose in each Case 1·0 Cubic Centimetre of Faecal Emulsion.

Number.	Date of Feeding.	Duration of Life.	Result.
2640	September 30, 1907	Killed 99 days	No tuberculosis.
2641		Killed 99 days	No tuberculosis.
2655	October 1, 1907	Killed 98 days	No tuberculosis.
2656		Killed 98 days	No tuberculosis.
2663	October 2, 1907	Killed 99 days	No tuberculosis.
2664		Killed 99 days	No tuberculosis.
2675	October 3, 1907	Killed 98 days	No tuberculosis.
2676		Killed 98 days	No tuberculosis.
2679	October 4, 1907	Died 60 days	No tuberculosis.
2680		Killed 98 days	No tuberculosis.
2690	October 5, 1907	Killed 98 days	No tuberculosis.
2691		Killed 98 days	No tuberculosis.
2698	October 7, 1907	Killed 98 days	No tuberculosis.
2699		Killed 98 days	No tuberculosis.
2706	October 8, 1907	Killed 98 days	No tuberculosis.
2707		Killed 98 days.	No tuberculosis.
2716	October 9, 1907	Killed 98 days	No tuberculosis.
2717		Killed 98 days	No tuberculosis.

GUINEA-PIGS FED CONTINUOUSLY WITH FAECES OF COW A MIXED WITH STERILIZED MILK.

Number.	Date of Feeding.	Duration of Life.	Result.
2629	From September 30, 1907, to October 9. 1907.	Killed 57 days	No tuberculosis.
2630		Killed 98 days	No tuberculosis.
2631		Killed 98 days	No tuberculosis.
2632		Died 5 days	No tuberculosis.
2633		Killed 106 days	No tuberculosis.
2634		Died 100 days	No tuberculosis.

PIG 204.

Fed with the faeces of Cow A from September 30, 1907, to October 9, 1907.

Dose—One-fourth part of 25·65 kilogrammes of faeces.

Age—11 weeks.

Killed in good health—December 30, 1907. [91 days after the experiment began.]

Weights.

	qrs.	lbs.
September 30, 1907	1	5
December 30, 1907	2	19

Gain in weight.—1 qr. 14 lb.

Tuberculin Tests.—September 16, 1907. [14 days before experiment began.] No reaction.

November 28, 1907. [59 days after the experiment began.] No reaction.

POST-MORTEM EXAMINATION.

General Condition.—Good. There was no tuberculosis of any organ or gland in the body.

PIG 206.

Fed with the faeces of Cow A from September 30, 1907, to October 9, 1907.

Dose—One-fourth part of 25·65 kilogrammes of faeces.

Age—11 weeks.

Killed in good health—January 7, 1908. [99 days after the experiment began.]

Weights.

	qrs.	lbs.
September 30, 1907	1	2
January 7, 1908	2	16

Gain in weight.—1 qr. 14 lbs.

Tuberculin Tests.—September 16, 1907. [14 days before the experiment began.] No reaction.

November 28, 1907. [59 days after the experiment began.] No reaction.

POST-MORTEM EXAMINATION.

Carcass in good condition. There was no sign of tuberculosis anywhere.

PIG 208.

Fed with the faeces of Cow A from September 30, 1907, to October 9, 1907.

Dose—One-fourth part of 25·65 kilogrammes of faeces.

Age—11 weeks.

Killed in good health—January 7, 1908. [99 days after the experiment began.]

Weights.

	qrs.	lbs.
September 30, 1907	1	3
January 7, 1908	2	20

Gain in weight.—1 qr. 17 lbs.

Tuberculin Tests.—September 16, 1907. [14 days before the experiment began.] No reaction.

November 28, 1907. [59 days after the experment began.] No reaction.

POST-MORTEM EXAMINATION.

Carcass in good condition.

There was no sign of tuberculosis anywhere.

PIG 210.

Fed with the faeces of Cow A from September 30, 1907, to October 9, 1907.

Dose—One-fourth part of 25·65 kilogrammes of faeces.

Age—11 weeks.

Killed in good health—December 5, 1907. [66 days after feeding began.]

Weights.

	lbs.
September 30, 1907	28
December 5, 1907	57

Total gain in weight.—29 lbs.

Tuberculin Tests.—September 16, 1907. [14 days before experiment began.] Reaction: Negative.

November 28, 1907. [59 days after the experiment began.] Reaction: Positive.

Rise of temperature—2·3° Centigrade.

POST-MORTEM EXAMINATION.

General Condition.—Good.

Tongue, Tonsils, Larynx, and Pharynx.—Normal.

On the Left Side of the Neck extending from below the angle of the jaw to the root of the ear, there was a chain of six glands the largest measuring 2·0 by 3·5 cm.; the smallest 1·6 by 1·2 cm. On section the largest consisted of a yellowish caseo-necrotic network in firm pinkish grey tissue. The other glands consisted of firm grey tissue with a fine yellowish network.

Right Submaxillary Glands.—Normal.

Cervical and Prescapular Glands.—Normal.

Abdomen.

Omentum and Peritoneum.—Normal.

Intestines.—Normal.

Mesenteric Glands.—The mesenteric glands were not enlarged and in one a single caseous focus was seen.

Spleen.—Normal.

Liver.—On the convex surface of the liver there were four grey tubercles with opaque centres up to a rape seed in size. On the concave surface there were two. On section through the substance no more were seen.

Portal Glands appeared normal.

Kidneys.—In the cortices of the kidneys there were scattered grey points.

Suprarenal Bodies.—Normal.

Renal, Coeliac, Lumbar, and Iliac Lymphatic Glands.—Normal.

Thorax.

Lungs.—In the left lung on the surface just beneath the pleura there were thirty caseating tubercles varying up to a hemp seed in size; there was about the same number on the right side; they were sparsely scattered throughout the parenchyma.

Bronchial Glands.—An occasional irregular caseous focus could be seen in the bronchial glands.

Precrural and Inguinal Glands.—Normal.

Microscopical Examination.

(Smear preparations.)

Kidney (grey foci).—Moderately numerous tubercle bacilli seen.

Mesenteric Gland (focus).—Eleven tubercle bacilli seen.

Bronchial Gland (focus).—No tubercle bacilli seen.

COW D.

POST-MORTEM EXAMINATION.

Animal fat and in good condition.

Thorax.

On opening the Thoracic Cavity there were numerous firm fibrous adhesions connecting the visceral and parietal pleurae. On the visceral side of these adhesions there were, in a majority of cases, nodules in the lung substance.

Lungs. Left Lung.—There was an adhesion between the anterior and the posterior lobes. The lung substance was pink and crepitant. The anterior lobe contained three nodules, the two largest the size of a sparrow's eggs; they consisted of yellow caseo-necrotic substance enclosed within fibrous capsules. In the posterior lobe there were eight large nodules varying from a large pea up to a mass 10·0 by 6·0 by 5·0 cm.; there were three nearly equal to the latter in size. On section they were composed of masses of yellow softening necrotic substance surrounded by fibrous walls. In the lung parenchyma, there were also seen scattered translucent tubercles with caseous centres varying up to a hemp seed in size.

Right Lung. — The anterior lobe contained five nodules up to a large pea in size and scattered translucent tubercles. The middle lobe contained a few nodules the largest the size of a pigeon's egg. The caudal lobe contained scattered nodules, about sixteen counted, varying in size up to a pigeon's egg, they all consisted of yellow caseo-necrotic substance in many cases becoming soft and purulent; there were also scattered minute translucent tubercles and nodules varying from a hemp seed up to a wheat grain in the substance. Several of the nodules were surrounded by pneumonic patches beset with caseous foci. A few of the softening nodules communicated with the smaller bronchi. Muco-pus could be squeezed from many of the bronchioles and soft caseous substance was seen in several of the larger bronchi.

Thoracic Lymphatic Glands. — The caudal mediastinal gland measured 24·0 by 7·0 by 5·0 cm. One half of it was much larger than the other and was firm and nodular. On section, the whole gland was replaced by bright yellow caseo-necrotic gritty masses, softening in many parts, disposed in a matrix of fibrous translucent tissue; the other mediastinal glands were a little enlarged and firm, and on section were more than half replaced by similar masses.

The bronchial glands were very slightly enlarged and resembled the mediastinal glands.

Abdomen.

Omentum.—Normal.

Intestines.—Normal.

Mesenteric and Colic Glands.—Normal.

Spleen.—Normal.

Liver.—In the centre of the liver there was a nodule of yellow caseo-purulent substance containing gritty foci lying in a bile duct with thickened walls.

Portal Glands.—Normal.

Kidneys.—Normal.

Suprarenal Bodies.—Normal.

Renal, Coeliac, Lumbar, and Iliac Glands.—Normal.

Ovaries and Uterus.—Normal.

Supramammary Lymphatic Glands.—Normal.

Udder.—Normal.

Tongue, Tonsils, Larynx, and Pharynx.—Normal.

Various Lymphatic Glands.

Parotid, Submaxillary, Pharyngeal, Cervical, Prescapular, Prepectoral, Axillary, Precrural, Gluteal, Ischiatic, and Popliteal Glands.—Normal.

Microscopical Examination.

(Smear preparation.)

Liver (pus).—No tubercle bacilli seen.

GUINEA-PIGS INOCULATED INTRAPERITONEALLY WITH A THICK EMULSION OF THE FAECES OF COW D.

Number.	Date of Inoculation.	Dose.	Duration of Life.	Result.
3017	February 20, 1908	·05 cc.	Killed 62 days	No tuberculosis.
3018		·05 cc.	Died 10 days	In the omentum there were several minute translucent tubercles containing moderately numerous tubercle bacilli.
3019		·05 cc.	Died 61 days	No tuberculosis.
3027	February 21, 1908	·05 cc.	Killed 61 days	No tuberculosis.
3028		·1 cc.	Killed 39 days	Three translucent foci and a small grey tubercle in omentum. No tuberculosis elsewhere. Smear from omentum showed moderately numerous acid fast bacilli.

GUINEA-PIGS INOCULATED INTRAPERITONEALLY WITH A THICK EMULSION OF THE FAECES OF COW D—*continued.*

Number.	Date of Inoculation.	Dose.	Duration of Life.	Result.
3133	March 24, 1908	·05 cc.	Died 14 days	No tuberculosis.
3134		·05 cc.	Died 3 days	No tuberculosis.
3135		·05 cc.	Killed 45 days	Early general tuberculosis. Culture isolated.
3136		·05 cc.	Died 4 days	No tuberculosis.
3137		·05 cc.	Killed 45 days	Caseation of pyloric and portal glands. Smear showed moderately numerous tubercle bacilli. Culture isolated.
3138		·05 cc.	Killed 45 days	No tuberculosis.

RABBITS INOCULATED INTRAPERITONEALLY WITH A THICK EMULSION OF THE FAECES OF COW D.

Number.	Date of Inoculation.	Dose.	Duration of Life.	Result.
1692	February 21, 1908	·05 cc.	Killed 82 days	Omentum contained caseating miliary tubercles. Caseous tubercles on diaphragm and in lungs. Caseation of pyloric and portal glands.
1693	February 21, 1908	·1 cc.	Killed 82 days	Omentum greatly thickened and caseated. Caseous nodules on caecum, mesentery, and diaphragm. Lungs closely filled with caseating tubercles. Tubercles in spleen and kidneys.
1694	February 21, 1908	·2 cc.	Killed 74 days	No tuberculosis.

GUINEA-PIGS INOCULATED INTRAPERITONEALLY WITH THE MILK OF COW D.

Number.	Date of Inoculation.	Dose.	Quarter of Udder.	Duration of Life.	Result.
3013	February 20, 1908	6·0 cc. plus the deposit 24·0 cc. obtained by the centrifuge.	R.F.	Died 26 days	Whitish tubercle in omentum containing moderately numerous acid fast bacilli. No tuberculosis elsewhere.
3014			R.H.	Died 21 days	No tuberculosis.
3015			L.F.	Killed 62 days	No tuberculosis.
3016			L.H.	Killed 62 days	No tuberculosis.
3037	February 24, 1908	do.	R.F.	Killed 35 days	No tuberculosis.
3038			R.F.	Killed 67 days	No tuberculosis.
3039			R.H.	Killed 35 days	No tuberculosis.
3040			R.H.	Killed 67 days	No tuberculosis.
3041			L.F.	Killed 58 days	No tuberculosis.
3042			L.F.	Killed 67 days	No tuberculosis.
3043			L.H.	Killed 58 days	No tuberculosis.
3044			L.H.	Killed 67 days	No tuberculosis.
3045	February 25, 1908	do.	R.F.	Died 2 days	No tuberculosis.
3046			R.F.	Died 62 days	Two translucent foci in omentum. No tuberculosis elsewhere.
3047			R.H.	Died 1 day	No tuberculosis.
3048			R.H.	Killed 66 days	No tuberculosis.
3049			L.F.	Killed 58 days	One translucent miliary nodule in the ligament of liver. No tuberculosis else.
3050			L.F.	Killed 66 days	No tuberculosis.
3051			L.H.	Died 58 days	Three tubercles in omentum; no T.B. No tuberculosis elsewhere.
3052			L.H.	Died 42 days	No tuberculosis.

GUINEA-PIGS INOCULATED INTRAPERITONEALLY WITH THE MILK OF COW D—*continued.*

Number.	Date of Inoculation.	Dose.	Quarter of Udder.	Duration of Life.	Result.
3087	March 13, 1908	60·0 cc. plus the deposit 24·0 cc. obtained by the centrifuge.	R.F.	Killed 50 days	No tuberculosis.
3088			R.F.	Died 6 days	No tuberculosis.
3089			R.H.	Killed 42 days	Two tubercles in omentum and two on peritoneum containing acid fast bacilli. No tuberculosis elsewhere.
3090			R.H.	Killed 50 days	No tuberculosis.
3091			L.F.	Killed 42 days	One yellowish nodule in omentum and one on liver containing acid fast bacilli. No tuberculosis elsewhere.
3092			L.F.	Killed 50 days	No tuberculosis.
3093			L.H.	Killed 43 days	No tuberculosis.
3094			L.H.	Killed 50 days	No tuberculosis.
3095	March 14, 1908	do.	R.F.	Killed 55 days	No tuberculosis.
3096			R.F.	Killed 55 days	No tuberculosis.
3097			R.H.	Died 29 days	Three translucent foci in the omentum. No tuberculosis elsewhere.
3098			R.H.	Killed 55 days	No tuberculosis.
3099			L.F.	Killed 55 days	No tuberculosis.
3100			L.F.	Killed 55 days	In omentum there was a yellowish miliary nodule containing soft caseous substance. Smear showed a few acid fast bacilli.
3101			L.H.	Killed 55 days	In omentum two similar but smaller nodules. Smear showed small acid fast bacilli.
3102			L.H.	Killed 55 days	Four similar bodies in omentum. Smear showed doubtful acid fast bacilli.
3103	March 16, 1908	do.	R.F.	Died 39 days	No tuberculosis.
3104			R.F.	Killed 47 days	No tuberculosis.
3105			R.H.	Killed 39 days	No tuberculosis.
3106			R.H.	Killed 47 days	No tuberculosis.
3107			L.F.	Killed 47 days	No tuberculosis.
3108			L.F.	Died 10 days	Three minute whitish tubercles in omentum containing acid fast bacilli. No tuberculosis elsewhere.
3109			L.H.	Died 39 days	No tuberculosis.
3110			L.H.	Killed 47 days	No tuberculosis.
3111	March 17, 1908	do.	R.F.	Killed 38 days	Purulent nodule in subcutaneous tissue showed no acid fast bacilli. No tuberculosis elsewhere.
3112			R.F.	Killed 42 days	No tuberculosis.
3113			R.H.	Killed 38 days	Purulent nodule in subcutaneous tissue containing numerous acid fast bacilli. No tuberculosis elsewhere.
3114			R.H.	Killed 42 days	No tuberculosis.
3115			L.F.	Killed 38 days	No tuberculosis.
3116			L.F.	Killed 42 days	No tuberculosis.
3117			L.H.	Killed 38 days	No tuberculosis.
3118			L.H.	Killed 42 days	In omentum three minute grey tubercles. No acid fast bacilli.
3125	March 23, 1908	do.	R.F.	Killed 43 days	No tuberculosis.
3126			R.F.	Died 6 days	No tuberculosis.
3127			R.H.	Died 1 day	No tuberculosis.
3128			R.H.	Killed 43 days	No tuberculosis.
3129			L.F.	Killed 32 days	No tuberculosis.
3130			L.F.	Killed 43 days	No tuberculosis.
3131			L.H.	Killed 43 days	No tuberculosis.
3132			L.H.	Died 27 days	No tuberculosis.

COW E.

POST-MORTEM EXAMINATION.

General Condition.—Good.

Thorax.

Pleura.—Normal.

Lungs.—In the right lung in close proximity to each other there were three loculated cystic nodules, the largest the size of a robin's egg; they were lined by reddish grey granulation tissue, and several of the small spaces in them contained a little muco-pus.

Thoracic Lymphatic Glands.—A left bronchial gland contained a soft grey nodule the size of a millet seed.

The long mediastinal gland contained 30 to 40 nodules varying up to a pea in size; they were yellowish caseo-calcareous and easily shelled out of the gland substance, leaving smooth walled cavities.

Abdomen.

Intestines.—Normal.

Gastric, Mesenteric, and Colic Glands.—Normal.

Spleen.—Normal.

Liver.—In the liver were sparsely scattered, irregular yellowish grey submiliary nodules situated just beneath the surface only; they were different from tuberculous nodules in appearance.

Portal Glands.—Normal.

Kidneys.—In the kidneys there were visible on the surface several pale grey patches of tissue which on section extended through the pyramids.

Suprarenal Bodies.—In a suprarenal body just beneath the cortex there was a yellowish grey nodule the size of a rape seed.

Abdominal Lymphatic Glands.

Renal, Lumbar, Coeliac, and Iliac Glands appeared normal.

Tongue, Tonsils, Larynx, and Pharynx.—Normal.

Uterus.—The uterus was pregnant and contained a foetus of about six months; the uterus, placenta, and foetus were normal.

Various Lymphatic Glands.

Submaxillary, Pharyngeal, Cervical, Prescapular, Axillary, Precrural, Gluteal, Ischiatic, and Popliteal Glands.—Normal.

Udder and Supramammary Lymphatic Glands.—Normal.

Microscopical Examinations.

(Smear preparations.)

Suprarenal (nodule).—Two tubercle bacilli.

Bronchial Gland (nodule).—No tubercle bacilli.

Lung (Cyst I and II).—No tubercle bacilli.

Liver (nodule).—No tubercle bacilli.

Kidney (grey patch).—No tubercle bacilli.

Mediastinal Gland (I and II).—No tubercle bacilli.

GUINEA-PIGS INOCULATED INTRAPERITONEALLY WITH THE FAECES OF COW E.

Number.	Date of Inoculation.	Dose.	Duration of Life.	Result.
3020	February 20, 1908	·05 cc.	Killed 62 days	No tuberculosis.
3021		·05 cc.	Killed 62 days	No tuberculosis.
3022		·05 cc.	Died 18 days	No tuberculosis.
3065	February 26, 1908	·05 cc.	Killed 57 days	No tuberculosis.
3066		·05 cc.	Died 2 days	No tuberculosis.
3067		·05 cc.	Died 1 day	No tuberculosis.
3068		·05 cc.	Died 1 day	No tuberculosis.
3081	March 13, 1908	·05 cc.	Killed 50 days	No tuberculosis.
3082		·05 cc.	Died 39 days	No tuberculosis.
3083		·05 cc.	Killed 50 days	No tuberculosis.
3084		·05 cc.	Killed 50 days	No tuberculosis.
3085		·05 cc.	Killed 53 days	No tuberculosis.
3086		·05 cc.	Killed 53 days	No tuberculosis.
3119	March 18, 1908	·05 cc.	Killed 51 days	No tuberculosis.
3120		·05 cc.	Killed 51 days	No tuberculosis.
3121		·05 cc.	Killed 51 days	No tuberculosis.
3122		·05 cc.	Killed 56 days	No tuberculosis.
3123		·05 cc.	Killed 56 days	No tuberculosis.

GUINEA-PIGS INOCULATED INTRAPERITONEALLY WITH THE MILK OF COW E.

Number.	Date of Inoculation.	Dose of Milk.	Quarter of Udder.	Duration of Life.	Result.
3023	February 21, 1908	6·0 cc. plus the deposit of 24·0 cc. obtained by the centrifuge.	R.F.	Died 59 days	No tuberculosis.
3024			R.H.	Killed 61 days	A translucent focus in omentum which contained acid-fast bacilli. No tuberculosis elsewhere.
3025			L.F.	Died 40 days	No tuberculosis.
3026			L.H.	Killed 61 days	No tuberculosis.
3029	February 24, 1908	do.	R.F.	Died 32 days	No tuberculosis.
3030			R.F.	Killed 67 days	No tuberculosis.
3031			R.H.	Died 35 days	No tuberculosis.
3032			R.H.	Died 62 days	No tuberculosis.
3033			L.F.	Died 41 days	No tuberculosis.
3034			L.F.	Died 63 days	No tuberculosis.
3035			L.H.	Killed 58 days	No tuberculosis.
3036			L.H.	Killed 67 days	No tuberculosis.
3053	February 25, 1908	5·0 cc. plus the deposit of 10·0 cc.	R.F.	Killed 58 days	No tuberculosis.
3054			R.F.	Killed 66 days	No tuberculosis.
3055		12·0 cc. plus the deposit of 12·0 cc.	R.H.	Died 18 days	No tuberculosis.
3056			R.H.	Died 21 days	No tuberculosis.
3057		10·0 cc.	L.F.	Killed 58 days	No tuberculosis.
3058			L.F.	Killed 66 days	No tuberculosis.
3059		5·0 cc. plus the deposit of 10·0 cc.	L.H.	Died 23 days	No tuberculosis.
3060			L.H.	Died 11 days	Two minute whitish foci in the omentum; smear showed acid-fast bacilli. No tuberculosis elsewhere.
3061	February 26, 1908	6·0 cc.	R.F.	Died 29 days	No tuberculosis.
3062		10·0 cc.	R.H.	Killed 57 days	No tuberculosis.
3063		6·0 cc.	L.F.	Died 16 days	Opaque yellowish nodule in subcutaneous tissue (no A.F.B.). No tuberculosis elsewhere.
3064		9·0 cc.	L.H.	Died 33 days	No tuberculosis.
3069	February 27, 1908	4·0 cc.	R.F.	Killed 64 days	No tuberculosis.
3070		4·0 cc.	R.F.	Died 16 days	No tuberculosis.
3071		7·0 cc.	R.H.	Killed 56 days	No tuberculosis.
3072		7·0 cc.	R.H.	Killed 64 days	No tuberculosis.
3073		3·0 cc.	L.F.	Killed 56 days	No tuberculosis.
3074		3·0 cc.	L.F.	Killed 64 days	No tuberculosis.
3075		3·0 cc.	L.H.	Killed 56 days	No tuberculosis.
3076		3·0 cc.	L.H.	Killed 64 days	No tuberculosis.
3077	March 3, 1908	6·0 cc.	R.F.	Killed 60 days	No tuberculosis.
3078		10·0 cc.	R.H.	Killed 60 days	No tuberculosis.
3079		8·0 cc.	L.F.	Killed 60 days	No tuberculosis.
3080		4·0 cc.	L.H.	Killed 60 days	No tuberculosis.

RABBITS INOCULATED INTRAPERITONEALLY WITH THE MILK OF COW E.

Number.	Date of Inoculation.	Dose of Milk.	Quarter of Udder.	Duration of Life.	Result.
1683	February 21, 1908	6·0 cc. plus the deposit of 24·0 cc. obtained by the centrifuge.	R.F.	Killed 85 days	No tuberculosis.
1684			R.H.	Killed 85 days	No tuberculosis.
1685			L.F.	Killed 85 days	No tuberculosis.
1686			L.H.	Killed 85 days	No tuberculosis.

SWINE FED CONTINUOUSLY WITH THE MILK OF COW D AND COW E.

Number.	Cow.	Duration of Feeding and Dose.	Duration of Life.	Result.
254	D	9 days, 7 litres each	Killed 88 days	No tuberculosis.
256	D		Killed 88 days	No tuberculosis.
250	E	4 days, 65·0 cc. each	Killed 88 days	No tuberculosis.
252	E		Killed 88 days	No tuberculosis.

SWINE FED CONTINUOUSLY WITH THE FAECES OF COW D AND COW E.

Number.	Cow.	Duration of Feeding and Dose.	Duration of Life.	Result.
238	D	14 days, 27 kilogrammes to each.	Killed 79 days	No tuberculosis.
240	D		Killed 99 days	No tuberculosis.
242	E	14 days, 21 kilogrammes to each.	Killed 79 days	No tuberculosis.
244	E		Killed 101 days	No tuberculosis.

CONTROL ANIMALS TO EXPERIMENTS ON SWINE.

PIG 220.

Reserved as a control to the litter to which belonged Pigs 204, 206, 208, 210, 212, 214, 216 and 218. The length of life of the experimental animals in this litter after the commencement of the experiment varied from 63 to 100 days.

Tuberculin test: September 16th, 1907. Result: Negative.

Killed: December 30th, 1907. Four months under observation.

Post-mortem examination: The animal was found to be healthy, and showed no sign of tuberculosis.

PIG 232.

Reserved as a control to the litter to which belonged Pigs 222, 224, 226 and 230. The experimental animals in this litter lived from 48 to 86 days after the commencement of the experiment.

Tuberculin test: October 11th, 1907. Result: Negative.

Killed: December 30th, 1907. After three months under observation.

Post-mortem examination: The animal was found to be healthy and showed no sign of tuberculosis.

The third litter contained Pigs 238, 240, 242, 244, 250, 252, 254 and 256. No control was kept, but all the experimental animals were found to be quite healthy when killed.

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ROYAL COMMISSION ON TUBERCULOSIS (HUMAN AND BOVINE).

FINAL REPORT

OF THE

ROYAL COMMISSION

APPOINTED TO INQUIRE INTO THE RELATIONS OF

HUMAN AND ANIMAL TUBERCULOSIS.

PART I.

REPORT.

Presented to both Houses of Parliament by Command of His Majesty.

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NEW ROYAL COMMISSION ON TUBERCULOSIS.

Edward R.

Edward the Seventh, by the Grace of God of the United Kingdom of Great Britain and Ireland, King, Defender of the Faith, To

Our Trusty and Well-beloved Sir Michael Foster, Knight Commander of Our most Honourable Order of the Bath, Doctor of Medicine, Fellow of the Royal Society, Professor of Physiology in Our University of Cambridge ;

Our Trusty and Well-beloved German Sims Woodhead, Esquire, Doctor of Medicine, Professor of Pathology in Our University of Cambridge ;

Our Trusty and Well-beloved Sidney Harris Cox Martin, Esquire, Doctor of Medicine, Fellow of the Royal Society, Professor of Pathology at University College, London ;

Our Trusty and Well-beloved John McFadyean, Esquire, Principal and Professor of Comparative Pathology and Bacteriology at the Royal Veterinary College ; And

Our Trusty and Well-beloved Rubert William Boyce, Esquire, Professor of Pathology at University College, Liverpool.

Greeting :

Whereas We have deemed it expedient that a Commission should forthwith issue to inquire and report with respect to Tuberculosis :—

1. Whether the disease in animals and man is one and the same ;
2. Whether animals and man can be reciprocally infected with it ;
3. Under what conditions, if at all, the transmission of the disease from animals to man takes place, and what are the circumstances favourable or unfavourable to such transmission.

Now know ye, that We, reposing great trust and confidence in your knowledge and ability, have authorised and appointed, and do by these Presents authorise and appoint you, the said Sir Michael Foster, German Sims Woodhead, Sidney Harris Cox Martin, John McFadyean, and Rubert William Boyce, to be Our Commissioners or the purposes of the said inquiry.

And for the better effecting the purposes of this Our Commission We do by these Presents give and grant unto you, or any three or more of you, full power to call before you such persons as you shall judge likely to afford you any information upon the subject of this Our Commission ; and also to call for, have access to, and examine all such books, documents, registers, and records as may afford you the fullest information on the subject, and to inquire of and concerning the premises by all other lawful ways and means whatsoever.

And We do by these Presents authorise and empower you, or any three or more of you, to visit and personally inspect such places as you may deem it expedient so to inspect for the more effectual carrying out of the purposes aforesaid.

And We do further by these Presents will and ordain that this Our Commission shall continue in full force and virtue, and that you, Our said Commissioners, or any three or more of you, may from time to time proceed in the execution thereof, and of every matter and thing therein contained, although the same be not continued from time to time by adjournment.

And We do further ordain that you, or any three or more of you, have liberty to report your proceedings under this Our Commission from time to time if you shall judge it expedient so to do.

And Our further Will and Pleasure is that you do, with as little delay as possible, report to Us under your hands and seals, or under the hands and seals of any three or more of you, your opinion upon the matters herein submitted for your consideration.

Given at Our Court at St. James's the Thirty-first day of August, 1901; in the first Year of Our Reign.

By His Majesty's Command.

CHARLES RITCHIE.

EDWARD R. & I.

EDWARD THE SEVENTH, by the Grace of God, of the United Kingdom of Great Britain and Ireland and of the British Dominions beyond the Seas King, Defender of the Faith, To

Our Trusty and Well-beloved WILLIAM HENRY POWER, Esquire, Companion of Our most Honourable Order of the Bath, Fellow of the Royal Society, Medical Officer of the Local Government Board,

GREETING:

Whereas by Warrant under Our Royal Sign Manual, bearing date the Thirty-first day of August, one thousand nine hundred and one, We were pleased to appoint Commissioners to inquire and report with respect to Tuberculosis, and to authorize the late Sir Michael Foster to act as Chairman of the Commission:

And whereas the Chairmanship of the Commission is at this present void.

Now know ye that We, reposing great trust and confidence in your knowledge and ability, have authorized and appointed, and by these Presents authorize and appoint you, the said William Henry Power, to be Chairman of the said Commission in the room of the said Sir Michael Foster, deceased.

Given at Our Court at Saint James's the Eighteenth day of March, 1907; in the seventh Year of Our Reign.

By His Majesty's Command.

H. J. GLADSTONE.

GEORGE, R.I.

George the Fifth, by the Grace of God, of the United Kingdom of Great Britain and Ireland and of the British Dominions beyond the Seas King, Defender of the Faith, to all to whom these Presents shall come,

Greeting :

Whereas it pleased His late Majesty from time to time to issue Royal Commissions of Enquiry for various purposes therein specified :

And whereas, in the case of certain of these Commissions, namely, those known as—

* * * * *

The Tuberculosis Commission,

* * * * *

the Commissioners appointed by His late Majesty, or such of them as were then acting as Commissioners, were at the late Demise of the Crown still engaged upon the business entrusted to them :

And whereas We deem it expedient that the said Commissioners should continue their labours in connection with the said enquiries notwithstanding the late Demise of the Crown :

Now know ye that We, reposing great trust and confidence in the zeal, discretion and ability of the present members of each of the said Commissions, do by these Presents authorise them to continue their labours, and do hereby in every essential particular ratify and confirm the terms of the said several Commissions.

And We do further ordain that the said Commissioners do report to Us under their hands and seals, or under the hands and seals of such of their number as may be specified in the said Commissions respectively, their opinion upon the matters presented for their consideration ; and that any proceedings which they or any of them may have taken under and in pursuance of the said Commissioners since the late Demise of the Crown and before the issue of these Presents shall be deemed and adjudged to have been taken under and in virtue of this our Commission.

Given at Our Court at *Saint James's*, the twenty-sixth day of *May*, one thousand nine hundred and ten, in the first year of our Reign.

By His Majesty's Command.

R. B. HALDANE.

CONTENTS.

REPORT.

Section I.—Three Types of Tubercle Bacillus.
  a. The Bovine Tubercle Bacillus.
  b. The Human Tubercle Bacillus
  c. The Avian Tubercle Bacillus.

Section II.—Bovine Tuberculosis.

Section III.—Human Tuberculosis.
  a. Cases other than Lupus.
  b. Lupus.

Section IV.—Swine Tuberculosis.

Section V.—Equine Tuberculosis.

Section VI.—Natural Tuberculosis in Mammals other than Man, Ox, Pig and Horse.

Section VII.—Avian Tuberculosis.

Section VIII.—Behaviour of Bacilli and fate of Bacilli in the Tissues of Animals Inoculated and Lesions produced.

Section IX.—Question of Modification of Bacilli and relation of Bacilli to each other.

Section X.—Results in relation to terms of reference.

SUPPLEMENTARY MEMORANDUM.

LIST OF REPORTS AND APPENDICES PRESENTED.

To THE KING'S MOST EXCELLENT MAJESTY.

May it please your Majesty,

We, your Majesty's Commissioners, appointed to inquire and report with respect to Tuberculosis :—

1. Whether the disease in animals and man is one and the same ;
2. Whether animals and man can be reciprocally infected with it ;
3. Under what conditions, if at all, the transmission of the disease from animals to man takes place, and what are the circumstances favourable or unfavourable to such transmission ;

humbly submit the following Final Report containing an account of the investigation we have carried out in accordance with the terms of our Reference and setting forth certain conclusions we have based on the results of our researches.

1. Three previous Reports have been issued by us. In the first (1904) the results of our preliminary investigations were discussed, and it was shown that the bacilli found in the lesions of certain cases of human tuberculosis produced in cattle a disease indistinguishable from bovine tuberculosis.

In our Second Interim Report (1907) we dealt at some length with bovine and human tuberculosis and embodied in it the results obtained up to that date in the investigation of the characters of the bacillus of bovine tuberculosis and of the bacilli found in cases of human tuberculosis.

In the Third Interim Report (1909) we dealt with certain conditions of the tuberculous cow which rendered her milk infective.

Since the second Report was presented we have continued our investigations into tuberculous disease of man and of the ox, and have also studied the tuberculosis which occurs in pigs, horses, some other mammals and birds. In this our final Report we propose to deal with the whole of our inquiry into the tuberculosis of all these various animals.

2. Our investigation has included the isolation of the bacilli from the lesions of the natural disease, the investigation of the cultural characters of the bacilli isolated and the study of their effects when introduced into different animals in varying doses and by several methods.

The species of animals used in this study have been cattle, rabbits, guinea-pigs, pigs, goats, chimpanzees, monkeys, horses, rats, mice, dogs, cats and birds. The experimental methods of infection employed have been subcutaneous, intravenous and intraperitoneal inoculation, and feeding. We have not attempted to infect by means of inhalation.

The experimental method of investigation we have adopted was essential in order to compare the characters of the bacilli isolated from the tuberculous lesions in different species of animals ; without it we should not have been able to give any answer to the questions referred to us.

We have necessarily made ourselves acquainted with the results published from time to time by others engaged in the study and experimental investigation of tuberculosis, but the conclusions arrived at in this Report are based solely on our own researches.

SECTION I.

Three Types of Tubercle Bacilli.

3. For purposes of description it is advantageous to distinguish three types of tubercle bacilli, recognisable by their individual characters. These are the human, bovine and avian types. The human type, although so named, is not the only one found in cases of tuberculosis in man. It is the organism present in the majority of such cases, but in some cases of the human disease the bacilli present are of the bovine type, and in others the bacilli have special characters distinguishing them from each of the three principal types. In natural cases of

tuberculosis in cattle the only type of bacillus present is the bovine type.* Similarly, in cases of natural tuberculosis occurring in poultry the bacillus belongs to the avian type.

The relationship between these three types of tubercle bacilli will be the subject of discussion in Section IX. At present only the individual characters of the three types will be described.

A.—The Bovine Tubercle Bacillus.

4. It will be convenient to take the bacillus of bovine tuberculosis as a standard for comparison with the bacilli found in the tuberculosis of other animals. The characters and properties of this bacillus have already been discussed in the Second Interim Report (2nd Int. Rep., page 6 *et seq.*) and it is unnecessary here to repeat many of the facts there recorded. But a summary of its behaviour will facilitate comparisons to be instituted between it and the bacilli of the tuberculous lesions of animals other than the bovine.

(a) *Cultural Characters.*—The bovine tubercle bacillus grows slowly on serum and at the end of two to three weeks shows on the surface of the medium a thin greyish uniform growth, not wrinkled and not pigmented.

2nd Int. Rep. p. 24.

In our Second Interim Report we divided the bovine tubercle bacillus into three grades or classes (I, II and III) according to the rate and luxuriance of its growth on glycerin media, Grade I growing the least and Grade III growing the most luxuriantly. We see no reason to alter this classification, but would insist from our further observations that this rate and kind of growth should not be taken as the sole basis of identification of the bacillus of bovine tuberculosis. The characters of the growth have to be considered in relation with the results of the inoculation of the bacillus before it can be stated that a particular tubercle bacillus is or is not a bovine tubercle bacillus.

2nd Int. Rep. Appendix, Vol. I.

(b) *Effects on Animals.*—The bovine tubercle bacillus produces characteristic effects when inoculated in certain doses into calves and rabbits, and it is these effects, taken with its mode of growth in artificial cultivation, that enable it to be recognised as such.

In calves the subcutaneous injection under the skin of the neck of 50 milligrammes of a culture of bovine tubercle bacilli not older than three weeks produces generalised tuberculosis starting from the point of inoculation and ending fatally usually within eight weeks. The nature of the acute disease produced has already been described in our Second Interim Report, and this statement may now be repeated (2nd Int. Rep., p. 7) :—

> "The local lesion is a mass of caseous tubercle, infiltrating the adjoining skin and muscle, and sometimes forming an abscess. The prescapular gland is a mass of caseous tubercle as is also the prepectoral gland, and as are also to a less but variable extent the thoracic and mediastinal glands. Tubercles more or less caseous are found in very many, sometimes in all, the other lymphatic glands. The lungs, spleen, liver, and also the kidneys are studded with tubercles, many of them caseous. Tubercles are found in the pleura, on the omentum, on the peritoneal surface, and in the intestinal walls."

The injection of this dose of the bovine tubercle bacillus causes severe general tuberculosis in the calf, and it is the result in this sense which we have taken as a standard of virulence for comparison with that of the other bacilli investigated.

It is true, as stated in our Second Interim Report (2nd Int. Rep., pp. 7 and 8), that definite tuberculosis may be produced in the calf by a much smaller dose than 50 milligrammes of culture of bovine tubercle bacilli. Some degree of tuberculosis has resulted in this animal from injection of so small an amount as 0·02 milligramme, while a dose no larger than 5 milligrammes has sufficed to cause generalised tuberculosis. This however, does not affect the statement already made as to the result produced by 50 milligrammes of culture.

In rabbits generalised tuberculosis ending in death within five weeks resulted from the intravenous inoculation of 0·01 or 0·1 of a milligramme of culture of bovine tubercle bacilli. With intraperitoneal injection in doses of 0·1 and 1 milligramme the duration of life was from 13 to 48 days, and 10 to 38 days, according to the dose, but with subcutaneous inoculation of doses of 10 milligrammes and

---

* In a calf inoculated subcutaneously with bacilli of the human type (H 79 JN), the avian bacillus was found in a nodule in a mesenteric gland. (Appendix Vol. I. Calf *1225*, p. 375.)

1 milligramme the duration of life was longer—28 to 101 days, and 29 to 165 days, according to the dose.

The disease caused in rabbits by intravenous injection is characterised by extensive miliary tuberculosis of the lungs, liver, spleen and kidneys, and other parts of the body. Intraperitoneal inoculation causes extensive tuberculosis of the peritoneum and abdominal lymphatic glands, extending afterwards into the internal organs. From subcutaneous inoculation there results a local lesion with tuberculosis of the neighbouring lymphatic glands, the lymphatic glands of the body, and the internal organs, especially the lungs and kidneys.

The results produced by injecting the bovine tubercle bacillus into calves and rabbits in the above doses are thus very striking and definite, and taken with the cultural characters of the bacillus afford a trustworthy means of recognising the bovine tubercle bacillus. Indeed, as our investigation progressed we found that it was sufficient to inoculate rabbits for differential diagnosis; for if an undetermined culture produces severe generalised disease in the rabbit within the period mentioned and by the doses referred to, administered in the various manners described, the same culture should produce an acute tuberculosis in the calf in doses of 50 milligrammes of culture subcutaneously inoculated. (*See* page 6.)

Other properties of the bovine tubercle bacillus may be mentioned. It invariably produces acute tuberculosis in the chimpanzee, monkey and guinea-pig, by subcutaneous inoculation in very small doses. In the goat, pig and cat generalised tuberculosis is also readily induced by it. Indeed, the results of an adequate dose in the goat, pig and cat have an equal value with those obtained in calves and rabbits in differentiating the bovine tubercle bacillus from the tubercle bacillus found in other kinds of tuberculosis. The rat and mouse are highly resistant to the subcutaneous inoculation of the bovine tubercle bacillus, but after intraperitoneal inoculation the tendency is for the bacillus to multiply in the body and to be present in large numbers in the organs, even in the blood, without causing the formation of tuberculous lesions such as are produced in animals susceptible to the bovine tubercle bacillus. The dog is highly resistant to the subcutaneous inoculation of the bovine tubercle bacillus but may succumb to general tuberculosis when large doses are inoculated intravenously or intraperitoneally.

In the fowl, the bovine tubercle bacillus injected intravenously causes death in about half the number of cases, usually with wasting of the bird, oedema of the lungs and pallor of the liver. In some cases the lungs show definite tubercles and the liver shows minute necrotic areas. Death is apparently caused by the toxic effect of the bacilli, as dead tubercle bacilli intravenously injected will produce the same effects as living. When injected intraperitoneally or intramuscularly, even in large doses, bovine bacilli produce in fowls only a local lesion, without dissemination of the disease.

In our experiments with horses the bovine tubercle bacillus in moderate doses did not produce progressive tuberculosis by subcutaneous inoculation or by feeding; given intravenously in a dose of 10 milligrammes, it caused the death of the animal from acute tuberculosis in 20 days.

Stability in Culture.—We have not found that the bovine tubercle bacillus diminishes in virulence to any great extent when subcultured for long periods—in one instance for as long as 1487 days. **Appendix, Vol. IV., pp. 391 & 434.**

B.—BACILLUS FROM CERTAIN CASES OF TUBERCULOSIS IN THE HUMAN BODY.

THE HUMAN TUBERCLE BACILLUS.

5. In our Second Interim Report (2nd Int. Rep., p. 14) we described the tubercle bacilli which we had found in cases of human tuberculosis and divided them into Groups (I, II, and III). Those belonging to Group I were proved to be identical with the bovine tubercle bacillus. The features of the bacilli of Group III were discussed, but final conclusions were not drawn by us regarding the significance of the somewhat anomalous results obtained. The bacilli of Group II had, however, definite characters and were obtained from the larger number of cases of human tuberculosis. This is the type of bacillus we have agreed to call the *human tubercle bacillus*, as it is the bacillus found in the majority of cases of human tuberculosis. What we stated in our Second Interim Report regarding this bacillus is confirmed by our further investigations. The chief characters of the bacillus are as follows:— **Appendix, Vol. I.** **Appendix, 2nd Int. Rep. Vol. II.**

(a) *Cultural Characters.*—The human tubercle bacillus grows more rapidly **2nd Int. Rep., page 26** than the bovine tubercle bacillus on serum, hence we have called it eugonic in contrast to the bovine bacillus, which is dysgonic. The growth tends to become wrinkled on glycerinated media, and becomes pigmented to a greater or less extent on all media.

(b) *Effects on Animals.*—It is in still greater contrast with the bovine tubercle bacillus when it is subjected to inoculation tests under the same conditions.

In calves, a subcutaneous inoculation of 50 milligrammes of a culture under three weeks old does not produce progressive tuberculosis in the animal, nor does it kill it. In the majority of instances the inoculation results in the formation of a local lesion, a larger or smaller mass, which may become a cyst, surrounded by a fibrous capsule: the lesion is thus retrogressive and localised. Lesions in the internal organs may occur, but these consist mainly of caseous or calcareous nodules in the lymphatic glands nearest the seat of inoculation, or of a few calcareous tubercles in various internal organs. In about half the number of experiments performed with this bacillus in 50 milligramme doses on calves, tuberculous lesions did not extend beyond the nearest glands, no lesions being found in the spleen, liver, or kidneys. It is quite clear therefore that the human tubercle bacillus possesses a much lower virulence for the calf than the bovine tubercle bacillus.

When inoculated into rabbits the contrast is also as a rule well-marked, so that, as previously stated, subject to certain precautions the rabbit test can be taken as a measure of virulence for calves; that is, if a bacillus is found slightly virulent for the rabbit it will be found slightly virulent also for the calf.

When the bovine tubercle bacillus is intravenously inoculated into rabbits in doses of 0·01 milligramme or 0·1 milligramme death occurs from acute and generalised tuberculosis within five weeks. With the human tubercle bacillus intravenously inoculated in doses of 0·1 to 1 milligramme, although the animals sometimes died in under 20 days, the majority lived for three months. Some died of tuberculosis of a chronic kind. The lungs may be free from lesions or may show only scattered grey fibrous or calcareous tubercles, or there may be fibrous nodules containing a little caseous matter. The kidneys usually show a few grey or caseous miliary tubercles. Besides the lungs and the kidneys, one or two glands are the only other parts usually affected. The liver and spleen are rarely tuberculous, but the eyes, genital organs, bones and joints, are sometimes diseased. This slowly progressive disease with limited lesions induced by intravenous injection of the human bacillus is in strong contrast with the acute generalised tuberculosis ending fatally within five weeks which results in the rabbit from the injection of similar doses of the bovine tubercle bacillus. When the bovine tubercle bacillus is injected into the peritoneal cavity of the rabbit the duration of life with a dose of 1 milligramme was 10 to 38 days; in the case of the human tubercle bacillus injected in doses of 1 milligramme the animals had survived for over three months before they were killed. After subcutaneous inoculation of the bovine bacillus in doses of 1 to 10 milligrammes the duration of life of the rabbit was from 28 to 65 days; with the human tubercle bacillus in doses of 1 to 100 milligrammes inoculated in the same way the animals survived or were killed in 94 to 725 days. Intraperitoneally and subcutaneously injected into rabbits the human tubercle bacillus produces lesions which are scattered, or localised and retrogressive.

Appendix, Vol. I, p. 38.

The above statement may be taken as generally correct. It has however been noted by Dr. A. Stanley Griffith that in certain cases intravenous inoculation of 1 milligramme or 0·1 milligramme of a culture of the human tubercle bacillus produced in rabbits an acute and rapidly fatal tuberculosis indistinguishable from that which was caused by the bovine tubercle bacillus, but that death from tuberculosis never occurred within three months when 0·01 milligramme was used as a dose, whereas such a dose of the bovine tubercle bacillus invariably produced a rapidly fatal tuberculosis in the rabbit. Dr. Griffith would therefore conclude that for the purposes of distinguishing between the bovine tubercle bacillus and the human tubercle bacillus by means of intravenous inoculation in the rabbit a dose of 0·01 milligramme should be used. With subcutaneous inoculation it was found that a dose of 10 milligrammes or more was a suitable one for the purposes of differential diagnosis. Such a dose of the bovine tubercle bacillus causes the death of the rabbit from acute generalised tuberculosis in 28 to 101 days, whereas with the human tubercle bacillus death does not occur from tuberculosis, and the animals have been killed in periods varying from 94 to 725 days.

The goat and the pig are not to any great extent affected by the human tubercle bacillus. In both animals the inoculation of this bacillus leads only to a slight retrogressive tuberculosis. Pigs perhaps are slightly more susceptible than calves. Acute tuberculosis is produced in the chimpanzee, monkey and guinea-pig by the human tubercle bacillus. The effect in the chimpanzee and monkey is similar to that which follows inoculation of like doses of the bovine tubercle bacillus. In the guinea-pig, however, the average duration of life is longer when the human tubercle bacillus is inoculated than after inoculation with the bovine tubercle bacillus. In the rat and mouse injected intraperitoneally with large doses of the human tubercle bacillus the bacilli become disseminated over the body, multiply in the tissues and cause death without producing characteristic tuberculous lesions. In the dog the human tubercle bacillus behaves like the bovine tubercle bacillus, that is, the animal is highly resistant to subcutaneous inoculation, but may die of generalised tuberculosis after intravenous or intraperitoneal inoculation of large doses.

The cat is resistant to the human tubercle bacillus when this is given subcutaneously, intraperitoneally, intramuscularly or by feeding. A few tuberculous lesions have been produced by intraperitoneal inoculation, but these were not widely distributed and did not affect the health of the animal.

In the fowl the effect of the human tubercle bacillus is similar to that of the bovine bacillus. In one experiment in a horse, the subcutaneous injection of 50 milligrammes produced only local disease.

Thus the human tubercle bacillus is distinguished from the bovine tubercle bacillus by its more ready growth on artificial media and by the results of its inoculation into rabbits, calves, cats, pigs and goats.

But both the bovine tubercle bacillus and the human tubercle bacillus are alike in that they readily produce tuberculosis in chimpanzees, monkeys and guinea-pigs, and in the circumstance that the lesions produced in these animals are the same in distribution and structure.

Stability in Culture.—The human tubercle bacillus has not shown any alteration in cultural characters on prolonged subcultivation.

C.—The Bacillus of Avian Tuberculosis.

6. Avian tuberculosis, as it occurs naturally in birds, is discussed in a separate section (VII). In this place an account is given of the characters and properties of the avian tubercle bacillus as exhibited under experimental conditions for comparison with those of the bovine tubercle bacillus and the human tubercle bacillus. **Appendix, Vol. IV, p. 167.**

(a) *Cultural Characters.*—The avian tubercle bacillus forms a slimy whitish growth, which is easily emulsified, thus contrasting with the growth of bovine and human tubercle bacilli. It grows especially well on glycerinated media.

(b) *Effects on Animals.*—The results of the inoculation of the avian tubercle bacillus into animals are in marked contrast with those obtained from inoculation of the bovine and the human tubercle bacillus.

Fowls are very susceptible to the action of the avian tubercle bacillus by intravenous, subcutaneous, and intramuscular inoculation, and by feeding. After inoculation there are tuberculous lesions in the spleen and liver, and frequently in the lungs, cervical glands, muscles, and bones. After feeding, the distribution of the lesions is the same, with the exception that characteristic tuberculous lesions are produced in the mucous membrane of the intestines.

The lesions produced by the avian tubercle bacillus in parrots do not differ from those produced in fowls ; but the avian bacillus, when introduced by feeding, does not cause lesions in the intestines of parrots so constantly as in fowls. Parrots are susceptible to the action of both the bovine and human tubercle bacillus, and when either of these is given by inoculation or by feeding the lesions set up are similar to those produced by the avian bacillus, the bovine tubercle bacillus being apparently more virulent for these birds than either the human or the avian tubercle bacillus.

The rabbit and mouse are the only two mammals in which the avian tubercle bacillus causes progressive tuberculosis.

In certain respects the results produced in the rabbit by the avian tubercle bacillus differ from those induced by bovine and by human tubercle bacilli. Moderately large doses of the avian bacillus, though fatal by inoculation to the rabbit, are less virulent than the bovine, but more virulent than the human tubercle bacillus.

It is, however, in the distribution of the lesions that the disease induced in the rabbit by the avian tubercle bacillus differs most markedly from the disease set up in this animal by either of the other two types of tubercle bacilli.

Intravenous inoculation of moderately large doses (1–10 milligrammes) leads to speedy death, with great multiplication of the bacilli in the organs, the only visible changes in which are general pallor with slight oedema of the lungs, and slight enlargement, with tubercles, of the spleen. If, however, the animal lives four or five weeks, the spleen is greatly enlarged owing to the formation of tubercles ; and these are seen also in the liver and to a less extent in the lungs. With a very small dose (·001 milligramme) the disease is very chronic and resembles the disease following subcutaneous inoculation, the joints being affected.

The disease set up in rabbits by subcutaneous inoculation of the avian bacillus in doses ranging from 50 milligrammes to a fraction of a milligramme is very chronic, and the distribution of the lesions is practically the same, irrespective of size of dose. Besides the local lesion the nearest lymphatic glands are implicated ; the liver and spleen are but rarely affected, while the amount of disease in the kidneys varies. The lungs are slightly oedematous and a few nodules may be seen on the surface. Caseating tubercles are seen in the areolar tissues and in a few of the lymphatic glands and in the testes. But the most characteristic and most commonly occurring lesion is a tuberculosis of the joints of the limbs which runs a chronic course. Joint tuberculosis may occasionally occur in the rabbit after intravenous inoculation with the human tubercle bacillus, but has not been observed after subcutaneous inoculation. It may, however, follow subcutaneous inoculation of the bovine bacillus, when the animal survives for a long period.

The distribution of the lesions in the chronic form of the disease in the rabbit therefore differs strikingly from that produced by the bovine and human tubercle bacillus.

Rabbits infected by feeding with the avian bacillus exhibit, besides the local lesion in the intestinal tract, a distribution of the lesions similar to that following subcutaneous inoculation. Intraperitoneal inoculation produces a tuberculosis similar to that following intravenous inoculation, the disease, however, being less acute.

In the mouse, a generalised tuberculosis is produced by the avian bacillus, whether this is inoculated subcutaneously or intraperitoneally or is given by feeding.

The calf, pig, monkey, guinea-pig, horse, cat, and rat behave alike to the avian bacillus, which in them never produces a progressive tuberculosis, though it sometimes multiplies in the body and becomes disseminated in the tissues and may kill if a large dose is given intravenously. The adult goat reacts similarly, resisting subcutaneous inoculation and feeding, although it succumbs to the effects of intravenous injection of the bacilli. Young goats are rather more susceptible than adults. The chimpanzee, in the single experiment performed, was found to resist a large dose (50 milligrammes of culture) of the bacillus injected subcutaneously and no tuberculous lesion was found when the animal died three years afterwards. In the dog, large doses injected intravenously produce no effects.

Appendix, Vol. IV., p. 178. *Vitality in Culture.*—The bacillus was found alive in culture after 1067 days.

Chemical Properties of the Three Types of Tubercle Bacilli.

Appendix, Vol. VI. 7. With a view to obtaining further data for differentiating tubercle bacilli of the several types, Dr. Harden undertook, as stated in our Second Interim Report, an investigation with the object of ascertaining what differences, if any, existed between them that could be detected by chemical means. This investigation, carried out by him with the assistance of Mr. Stanley Walpole at the Lister Institute, occupied a considerable time ; the results are set out in Dr. Harden's Report, containing full details of his experiments, which forms a separate volume of our Appendix.

For the purpose of this Section it is sufficient for us to state that although certain minor points in which tubercle bacilli of one type differed slightly but not always uniformly from those of another were noted, such differences appeared to be due rather to the amount and rapidity of growth in artificial culture than to any fundamental differences in the chemical properties of the bacilli themselves.

Dr. Harden was unable to detect any definite and constant bio-chemical character by which tubercle bacilli of one type can be differentiated from those of another.

SECTION II.

Bovine Tuberculosis.

8. In our Second Interim Report the investigation of 30 cases of bovine tuberculosis was recorded. No further special investigation of cases of bovine tuberculosis has been made as the results already obtained were definite. Only one form or type of tubercle bacillus was found in these cases, the bacillus having the cultural and pathogenic characters repeated in detail in our present Report.

SECTION III.

Human Tuberculosis.

9. In our Second Interim Report the results obtained in the investigation of the bacilli isolated from 56 cases of human tuberculosis were recorded, as also the results of the investigation of the infectivity of mixed sputum. Other cases have since been investigated, and these will now be discussed together with those previously recorded in our Second Interim Report. It will be convenient, for reasons which will presently appear, to discuss these cases under two headings : (a) Cases of Human Tuberculosis other than Lupus ; (b) Cases of Lupus.

Appendix, Vols. I & II.

2nd Int. Rep., Appendix. Vol. II.

CASES OF HUMAN TUBERCULOSIS OTHER THAN LUPUS.

10. These cases, 108 in number, are arranged as regards the primary seat of disease as far as this could be ascertained. The results obtained are shown in the table on the following pages. The arrangement of the table differs from that used in our Second Interim Report, inasmuch as the viruses obtained from these different cases are now classified according as they are bovine, human, or mixed (bovine and human). The classification here given must be considered as embodying the final results of our investigation of the cases under consideration.

Appendix, Vol. I.

2nd Int. Rep., Appendix, Vol. II.

On comparing this Table with the details given in the Appendix an apparent discrepancy in the relative numbers will be found, and a brief explanation is therefore necessary. The total 108 is the number of individual cases of tuberculosis (other than Lupus) occurring in the human subject on which we have based our final conclusions, but it is not the total number of separate " viruses " of human tuberculosis examined by us and reported in the Appendix. Viruses H 2 and H 17 are not included in the Table because they did not represent individual cases but were viruses consisting of mixed sputum from a varying number of cases of human pulmonary tuberculosis ; they are, however, separately considered later in this Report. In the preface to Volume II of the Appendix to our Second Interim Report it was stated that a virus provisionally numbered H 60 had not been included in that Report as there appeared to be a possibility that the material might have been accidentally contaminated. Subsequent experience proved that this misgiving was without foundation, and the case is now included amongst the 108 in this Table. A few viruses included in the Appendix to the Second Interim Report are altogether omitted from further consideration. Of these, H 1, H 4, and H 6 were early experiments which appear now to have been incomplete. H 62 and H 147, viruses consisting of sputum from separate patients are omitted because precautions afterwards adopted in collecting sputum had not been taken. Another virus, H 150, is left out as no cultures were isolated. One case numbered Virus H 24 in the Appendix to our Second Interim Report, and certain others the details of which are summarised on page 18 of Volume I of our Appendix to this Report, are omitted from further consideration and not included in this Table because the material yielded no culture and failed to give rise to tuberculosis when injected into guinea-pigs.

CASES OF HUMAN TUBERCULOSIS OTHER THAN LUPUS.

(108 Cases.)

TABULAR SUMMARY OF RESULTS.

Nature of Case.	Part from which Experimental Material was obtained.	Bovine Viruses (Group I).	Human Viruses (Group II).	Mixed Viruses (Bovine and Human).
I.—(A) Primary Pulmonary Tuberculosis (14 Cases).	Lung ... ... Thoracic Gland ...	—	H 22. “F.W.”	
	Lung	—	H 23. “J.P.”	
	”	—	H 25. “A.T.”	
	Bronchial Gland ...	—	H 45. “F.M.”	
	Lung	—	H 48. “W.P.”	
	”	—	H 50. “P.H.”	
	”	—	H 51. “H.M.”	
	”	—	H 52. “T.F.”	
	”	—	H 56. “F.T.”	
	Lung ... ... Cervical Gland ...	—	H 58. “F.G.”	
	Lung	—	H 79. “J.N.”	
	”	—	H 80. “D.M.”	
	Lung ... ... Spleen	—	H 81. “P.W.”	
	Lung .. ... Mesenteric Gland...	—	H 104. “E.R.”	
(B) Sputum from Individual Cases of Pulmonary Tuberculosis (28 Cases).	Culture from Sputum	H 127. “R.R.” H 128. “D.D.”	H 118–126 (9 Cases). H 129–145 (17 Cases).	
II.—General Tuberculosis (3 Cases).	Bronchial Glands...	—	H 35. “C.B.”	
	Lung ... ... Acne Spots... ...	—	H 93. “C.D.”	
	Lung ... ... Meninges ... ... Bronchial Gland ...	—	H 78. “O.D.”	
III.—Tuberculous Meningitis (3 Cases).	Meninges	—	H 86. “C.P.”	
	Cerebro-spinal Fluid	—	H 98. “B.R.”	
	” ”	—	H 115. “N.G.”	
IV.—Bronchial Gland Tuberculosis (5 Cases).	Bronchial Gland ...	—	H 21. “G.B.”	
	Spleen	—	H 54. “C.W.”	
	Mesenteric Glands Meninges	—	H 61. “E.C.”	
	Bronchial Glands and Spleen.	—	—	H 13. “A.D.”
	Bronchial Gland ... Meninges ... ... Lung ... ... Mesenteric Gland...	—	—	H 60. “W.B.”
V.—Cervical Gland Tuberculosis (9 Cases).	Cervical Glands ...	H 28. “C.L.” H 29. “M.F.” H 31. “L.F.”	H 27. “B.D.” H 34. “C.U.” H 37. “O.J.” H 39. “M.B.” H 44. “D.C.”	
	Axillary Glands ...	—	H 33. “R.T.”	

Cases of Human Tuberculosis other than Lupus—*continued.*

Nature of Case.	Part from which Experimental Material was obtained.	Bovine Viruses (Group I).	Human Viruses (Group II).	Mixed Viruses (Bovine and Human).
VI.—Primary Abdominal Tuberculosis (29 Cases).	Mesenteric Glands	H 7. "C.M." H 10. "B.S." H 14. "F.S." H 19. "S.W." H 20. "F.L." H 65. "K.B." H 88. "E.L."	H 8. "S.C." H 12. "H.N." H 18. "T.T." H 55. "R.D."	H 49. "T.C."
	Mesenteric and Bronchial Glands.	—	H 30. "E.M."	
	Mesenteric Glands Bronchial Glands ...	—	H 36. "M.D."	
	Cervical Gland ...	H 38. "J.M."		
	Mesenteric Glands Lung	—	H 57. "B.J."	
	Mesenteric Gland... Cervical Gland ... Brain	—	H 63. "G.R."	
	Mesenteric Gland... Lung ... ... Bronchial Gland ...	H 32. "Y.W."		
	Mesenteric Gland... Lung ... ... Cervical Gland ... Brain	H 59. "L.B."		
	Mesenteric Gland... Retro-peritoneal Gland.	—	—	H 90. "I.P."
	Mesenteric Gland... Meninges	H 64. "M.G."		
	Mesenteric Gland ... Meninges	H 69. "F.K."		
	Cervical Gland ... Mesenteric Gland ... Lung ... ... Bronchial Gland ...	—	H 70. "N.W."	
	Mesenteric Gland... Bronchial Gland ... Lung ... ... Spleen	—	H 74. "D.S."	
	Peritoneal Fluid ... Lung	—	H 75. "A.H."	
	Mesenteric Gland... Liver	H 77. "R.L."		
	Mesenteric Gland... Lung	—	H 82. "G.F."	
	Mesenteric Gland... Bronchial Gland ...	—	H 83. "G.C."	
	Mesenteric Gland... Lung	H 89. "W.I."		
VII.—Joint and Bone Tuberculosis (14 Cases).	Scrapings from Joints	—	H 9. "C.T." H 11. "E.D." H 15. "I.W." H 41. "A.S." H 42. "M.R." H 43. "F.F." H 46. "H.W." H 47. "S.B." H 76. "G.M."	*H 16. "J.H."
	Lumbar Abscess ...	—	H 66. "W.C."	
	Scapular Abscess ...	—	H 67. "E.P."	
	Sacral Abscess ...	—	H 68. "R.B."	
	Rib Abscess ...	—	H 72. "H.C."	
VIII.—Tuberculosis of Testicle. of Kidney. of Suprarenal. (1 case of each.)	Testicle	—	H 40. "J.G."	
	Kidney	—	H 26. "K.M."	
	Suprarenal... ...	—	H 87. "W.D."	

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* H 16. "J.H." is discussed in the text (p. 15).

11. *Cases of Pulmonary Tuberculosis.*—These fall into two series. In the first series (14 cases) a portion of the tuberculous lesion obtained at the post-mortem examination was used for investigation. In 13 of the cases this was the lung, in the other a bronchial gland only was used. In addition to the lung, a thoracic gland in one case, a cervical gland in a second case, a mesenteric gland in a third, and the spleen in a fourth, were investigated. These were clinically all cases of primary pulmonary tuberculosis, the disease which is commonly called consumption, in which the main and seemingly primary tuberculous lesion was in the lung, and in which death resulted from the pulmonary disease. In all these 14 cases the bacillus found was the human tubercle bacillus, and no evidence of the presence of the bovine tubercle bacillus was obtained.

Appendix, Vol. I, p. 8. The second series of cases included those in which sputum alone was examined. The sputum from 28 cases was used. The patients were usually young adults, and each case was investigated separately. To meet the possibility of the sputum being mixed with bovine bacilli derived from milk or butter the following precautions were taken :—Twenty-four hours before the collection of the samples of sputum the teeth and gums of the patient were carefully cleansed, and the mouth washed out repeatedly. Subsequently the patient was not allowed to take any milk or milk product until after the sputum had been collected. It was received directly into sterilised wide-mouthed bottles, and was then sent for investigation. Guinea-pigs were inoculated with the sputum and cultures obtained from them. In two cases cultures were also obtained direct from the sputum.

As regards the patients themselves, nineteen were aged 16 to 25, eight were aged 26 to 33, and one was 50 years old. Twenty-six were males, and two females. In 8 cases the disease had lasted 12 months or less ; in 16 cases, from 1 to 3 years ; in one case, 4 years, in one 5, and in another 7, and one was of doubtful duration. The stage of the disease at which the sputum was collected was noted as far as could be detected by physical signs. In 12 cases there were signs of excavation of the lungs, or cavity formation, and in 16 cases there were signs of consolidation of the lungs on one or both sides, but with no signs of cavity formation. In no case could any evidence be found of disease except in the lungs.

The results of the investigation of these cases showed that the living tubercle bacilli present in the sputum in 26 cases were human, and in 2 cases were bovine. In none of the cases was there a mixture of bovine and human tubercle bacilli.

Appendix, Vol. I, p. 9. The two cases which showed only bovine bacilli in the sputum deserve special notice. The cultures in these two cases grew like bovine bacilli on artificial media and gave rise to fatal generalised tuberculosis in both calves and rabbits. There was no evidence of the presence of eugonic human bacilli in the sputum. One examination in these cases was not considered sufficient. From one of the patients, H 127. " R.R." additional specimens of sputum were collected on three separate occasions at intervals of 76, 117, and 118 days after the collection of the first specimen. Cultures were obtained direct from the sputum. The investigation of these three specimens gave the same results as the first. The sputum yielded only bovine tubercle bacilli. From the other patient, H 128. " D.D." one additional specimen was obtained 118 days after the first. This, like the first, yielded only bovine tubercle bacilli, which were isolated from the sputum direct and produced fatal tuberculosis in calves and rabbits. These two cases were therefore definite cases of pulmonary tuberculosis caused by bovine tubercle bacilli, and as far as could be ascertained during life they were cases of primary pulmonary tuberculosis. In neither of the patients was there any evidence of tuberculous disease elsewhere, such as disease of the cervical glands or of the intestinal tract when the sputum was collected.*

12. In three cases of *general tuberculosis*, the primary lesion of which could not be determined, and in three cases of *tuberculous meningitis*, in which the meninges and cerebro-spinal fluid were used for investigation, the lesions yielded human tubercle bacilli only.

13. *Bronchial gland tuberculosis* :—Five cases were examined. Three of these yielded human tubercle bacilli. Two others, H 13. " A.D." and H 60. " W.B.", contained each a mixture of bovine tubercle bacilli and human tubercle bacilli. These two kinds of bacilli were separated and their characters investigated. (*See* page 15.)

14. Nine cases of *cervical gland tuberculosis* in which the tubercle bacilli were

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*** Both these patients subsequently died ; the cause of death in one case was stated to have been phthisis, and in the other was apparently general tuberculosis with intestinal ulceration. No post-mortem examination could be obtained in either case.**

obtained from specimens removed by operation were examined. Of these six yielded human tubercle bacilli and three bovine tubercle bacilli.

15. *Primary abdominal tuberculosis*, twenty-nine cases in all. Of these, 14 yielded bovine tubercle bacilli, 13 human tubercle bacilli, and two cases were proved each to contain a mixture of bovine tubercle bacilli and human tubercle bacilli. The ages of the patients were as follows : In the bovine cases, ten were aged 1 to 3 years ; three, from 4 to 5 years ; and one, 8 years ; in the human cases, eight were aged 1 to 3 years ; three, from 3 to 5 years ; one, 7 years and one 15 years. The causes of death in the bovine cases were as follows : 11 died of tuberculosis, either of the generalised disease (6), of tuberculous peritonitis (2), or of meningitis (3) ; 2 died of intestinal obstruction following cicatrization of the gut, and one died of non-tuberculous pneumonia. The causes of death in the human cases were as follows : 12 died of tuberculosis, and one of streptococcal pericarditis and pleurisy.

Of the 14 cases found to be bovine the mesenteric glands in seven instances and the cervical glands in one instance were alone investigated. In the remaining six of these 14 other lesions besides the mesenteric glands were in each instance subjected to scrutiny, as follows :—Mesenteric glands and meninges, two cases ; mesenteric glands, lung and bronchial glands, one case ; mesenteric glands and liver, one case ; mesenteric glands and lung, one case ; and mesenteric glands, cervical glands, lung and meninges, one case. In such cases as these there can be little doubt that the tubercle bacillus entered the system through the intestinal tract, affecting first the mesenteric glands and subsequently other parts of the body ; and inasmuch as in the six cases in this category which supplied each a plurality of lesions for examination only one type of tubercle bacillus was found, whether in lesions near or in lesions remote from the point of entry, it is to be inferred that the persons, all of them children, died as a result of infection with bovine tubercle bacilli.

All cases of abdominal tuberculosis are not however caused by infection with the bovine type of tubercle bacillus. Of the 15 such cases in which a plurality of lesions was in each instance tested on exactly parallel lines, nine yielded none but human tubercle bacilli. In the remaining 12 cases of abdominal tuberculosis in regard of which a single lesion in each instance (mesenteric gland or cervical gland) was alone examined, four yielded human and no less than eight yielded bovine bacilli.

The two remaining cases in this group showed a mixture of bovine and human tubercle bacilli. In one case, a youth aged 18 years who died of pulmonary tuberculosis, the mesenteric glands alone were investigated. In another, an old man aged 70 years who died of pneumonia, the mesenteric glands and the retro-peritoneal glands were investigated (*See* page 15).

16. *Joint and bone tuberculosis.*—Fourteen cases. The cases illustrate very fairly the different forms of "primary" bone and joint tuberculosis occurring in man. The material used from ten consisted of scrapings from joints ; in four pus from bone abscesses was used. Thirteen of these cases yielded the human tubercle bacillus only. The circumstances relating to one case, H 16. "J.H.", were peculiar and are discussed later (page 15).

17. One case of tuberculosis of the *testicle*, one of the *kidney* and one of the *supra-renal capsule* were investigated. They each yielded human tubercle bacilli only.

18. Of the total of 108 cases of human tuberculosis investigated 84 yielded human tubercle bacilli only, 19 yielded bovine tubercle bacilli only, and five both bovine and human tubercle bacilli. Although the bovine tubercle bacillus may, as it appears, be solely responsible for certain cases of pulmonary tuberculosis (consumption) and though it may be present with the human tubercle bacillus in the bronchial glands, it is evident from the data recorded that the majority of cases in which the bovine tubercle bacillus is the infective agent in the human being are cases of alimentary tuberculosis. Such are cases of cervical gland and primary abdominal tuberculosis. In the latter class of cases at least the tubercle bacillus has unquestionably been swallowed. Received in this way the tubercle bacillus, whether human or bovine, may pass through the pharyngeal or buccal mucous membrane and infect the cervical glands, or getting into the small intestine it may produce several different lesions such as ulceration of the gut, tuberculosis of the mesenteric glands attached and of the peritoneal covering. The percentage of these cases of alimentary tuberculosis due to the bovine tubercle bacillus is very large. Taking both classes of cases (cervical gland and abdominal) together, numbering 38, there are 17 in which the bovine bacillus alone was found, 19 in which the human bacillus alone was found, and two in which both were found. Taking the

primary abdominal cases alone it is seen that in 16 out of 29 the bovine bacillus was found; in 14 of these it was the sole infective agent present.

*Mixed Viruses in Human Tuberculosis.**

19. In our Second Interim Report we recorded the results of feeding two sets of bovine animals with large quantities of mixed sputum, the experiments being designated respectively Virus H 2. "Sp. A." and Virus H 17. "Sp. B."

In the experiments with H 2 "Sp. A." one of two heifers which had been fed with the sputum for 209 days was killed at the end of that period and found to have only a few calcareo-caseous tuberculous lesions in the mesenteric and hepatic glands. The bacilli from these glands, which had been passed on into calves and guinea-pigs in an emulsion of the tissues, were found to possess the cultural characters of the bovine tubercle bacillus and the high virulence of that bacillus for the calf and rabbit. In the other heifer, fed with mixed sputum for 300 days, retrogressive calcareous tubercles were found in the mesenteric glands; and emulsion of these glands produced in one calf limited retrogressive tuberculosis, but the same emulsion passed through a guinea-pig produced in another calf fatal progressive generalised tuberculosis.

Re-investigation of two of the cultures of this virus which still existed has not added more to our knowledge than was available at the time of the issue of the Second Interim Report, but in the light of more extended observations on other viruses and of new facts acquired during their investigation we are now of the opinion that the results obtained are to be accounted for by the presence in the human sputum as used for feeding of a small number of bovine tubercle bacilli.

With regard to the second sputum experiment (H 17. "Sp. B."), the virus, which we placed in Group III., was slightly virulent at first and became virulent afterwards, but only in one of the four series of animals through which the virus was passed. The tuberculous material consisting of mesenteric glands from one of the four calves with which the several series began, after passing through two guinea-pigs in succession, was injected subcutaneously in the form of an emulsion into a calf (Calf *339*). It produced a limited retrogressive tuberculosis and a culture from the tuberculous organs of this calf (through a guinea-pig) was eugonic and exhibited low virulence for calves and rabbits. Clearly the virus up to this point possessed the characters of the human tubercle bacillus. Tuberculous material from Calf *339* was injected intravenously in the form of an emulsion into a second calf, and from this animal also intravenously and in the form of an emulsion successively into a third, fourth, and fifth calf. A culture derived from the last calf of the series was dysgonic and highly virulent. But a culture isolated from a rabbit which had been inoculated with material from one of the intermediate calves was eugonic and at first virulent; after 16 months cultivation it was found to have no higher virulence than the human tubercle bacillus. This strain was tested again after a still longer period of subcultivation and was proved to be composed of slightly virulent eugonic bacilli only.

The result obtained with this virus is not so readily explained as in the case of H 2. "Sp. A.", on the assumption that the original material (the sputum) contained bovine as well as human tubercle bacilli, and the appearance of bovine tubercle bacilli might possibly have been the consequence of an accidental contamination of one of the calves during the course of the experiment. On the other hand it might be suggested that the bovine bacilli were present in the sputum in such small numbers that they became lodged in one only of the four calves fed with it and needed several passages through animals before they became so increased in numbers as to be able to produce their characteristic pathogenic effects.

Though in mixed sputum from many cases of pulmonary tuberculosis the majority of bacilli present are doubtless human tubercle bacilli, it is always possible that one or more of a group of phthisical patients may contribute sputum containing besides the human bacillus bacilli of the bovine type. We have shown indeed that cases of pulmonary tuberculosis (H 127 and H 128) can supply sputum yielding no other tubercle bacillus than the bovine.

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* For the details of the original investigation of certain of these viruses *see* Vol. II. of the Appendix to the 2nd Interim Report. The results of those investigations are discussed by Dr. Cobbett in a Report submitted by him to the Commission in 1906 and now included in the Appendix to this Report (Vol. III). Recent work by Dr. A. Stanley Griffith on these and other similar viruses will be found in Vol. III of the Appendix, p. 5.

20. Five other viruses which presented anomalous features remain for special consideration ; three of these were discussed in our Second Interim Report (H 13. "A.D.", H 49. "T.C.", H 16. "J.H.") ; two others (H 60. "W.B." and H 90. "I.P.") were investigated after that Report was published. Those previously described in our Second Interim Report and placed in a group (Group III) by themselves were viruses which, after animal passage, became more virulent for calves and rabbits. We came, in that Report, to no definite conclusion as to the interpretation of the experiments recorded, but suggested two possible explanations. The first was that the results were due to a mixture of bacilli, the bovine tubercle bacillus and the human tubercle bacillus, and that during the passage through the series of calves the human bacillus was lost owing to the fact that the tissues of the calf are hostile to the growth of this bacillus, the bovine bacillus persisting meanwhile in the tissues of the calf and finally, in appropriate doses, setting up fatal generalised tuberculosis in that animal. The second possible explanation discussed by us was that the cases might be examples of modification, that the eugonic human bacillus, introduced successively into a series of calves, might have become modified into the dysgonic bovine bacillus. 2nd Int. Rep., p. 30.

The subject appeared one of such great importance that special investigations were undertaken by Dr. A. Stanley Griffith to determine whether the cultures used were mixtures of the two kinds of bacillus, and the procedure adopted may be shortly described. Appendix, Vol. III.

In a mixture of bovine and human tubercle bacilli separation of the two types of bacillus may be effected in one or other or all of three ways :—(1) By passing the culture through the bodies of animals, for example calves and rabbits, which permit the multiplication of the bovine bacillus and resist that of the human bacillus ; (2) by sub-culturing on a glycerin medium which is more favourable to the growth of the human bacillus than to that of the bovine bacillus ; (3) by sowing the culture to be tested on the flat surface of a medium on a plate, on which any individual colonies that develop can be seen and separated for investigation.

These experiments were successful in showing that in viruses H 13. "A.D.", H 60. "W.B.", H 49. "T.C.", and H 90. "I.P.", two cases of bronchial gland tuberculosis and two cases of abdominal tuberculosis, the tested cultures were a mixture of the bovine bacillus and the human bacillus. Thus Virus H 13. "A.D.", which in culture was eugonic though virulent, after inoculation into calves and rabbits, grew like a bovine bacillus, the eugonic element or human bacillus having been in this way eliminated. By plate cultivation of the eugonic tubercle bacillus from a passage Calf (*301*) in this series two sorts of colonies were obtained, one like the bovine bacillus, the other like the human bacillus. In the case of Virus H 60. "W.B." the bovine bacillus was separated by animal inoculation from the human bacillus ; by plate culture both the human bacillus and the bovine bacillus were isolated. A similar result was obtained with Virus H 49. "T.C." and with Virus H 90. "I.P."

Viruses H 13. "A.D." and H 49. "T.C.", therefore, are not to be regarded as instances in which the slightly virulent human bacillus became transformed in the body of the calf into the dysgonic virulent bovine bacillus. On the contrary the anomalous results recorded in our Second Interim Report are to be explained by the fact that the viruses each contained two elements, the bovine tubercle bacillus and the human tubercle bacillus.

There remains one virus for consideration, viz., Virus H 16. "J.H." This was obtained from the knee-joint and was one of those which, as stated in our Second Interim Report, was at first only slightly virulent but became on passage highly virulent. When slightly virulent the cultures were eugonic, that is, were like the human tubercle bacillus, but in the later stages of the passage when the cultures were virulent they were dysgonic and like the bovine tubercle bacillus. The cultures of this series which were available for re-investigation after a lapse of 2½ to 3 years did not yield results different from those obtained in the first investigation ; that is, one culture from the earlier calf in the passage was eugonic and non-virulent, whilst two cultures from animals later in the series were dysgonic and virulent. It is quite clear therefore that in the case of H 16 we were dealing with two different kinds of cultures, the human tubercle bacillus and the bovine tubercle bacillus ; and so far it may be concluded that the virus was a mixed one. As an original culture of the virus was not available for investigation we were unable to determine by experiment whether this particular virus was a mixture or not.

Cases of Lupus.

Appendix, Vol. II.

21. Cases of lupus are considered separately from the other cases of human tuberculosis for the reason that they present certain divergent features of particular interest.

The cases of tuberculosis which have already been considered are those in which the disease affected the internal parts of the body: the internal organs, glands, joints or bone. In lupus the tuberculosis is usually limited to the skin. It runs as a rule a very chronic course and is not commonly associated with internal tuberculosis. It may persist for many years without any sign of disease in the lungs or other parts of the body, and indeed even the lymphatic glands near the area of skin affected by lupus are not usually tuberculous.

22. The investigation was conducted with great care and completeness by Dr. A. Stanley Griffith. Twenty* cases of lupus were examined, one of which (H. 53) was referred to in our Second Interim Report. Of these cases fourteen were females and six were males. The ages of the patients when they first came under our observation were as follows: from 4 to 10 years of age, three females and four males; from 10 to 20 years, five females and two males; from 20 to 40 years, four females; and two females were aged 53 and 68 respectively. The site of the lupus varied considerably. In two cases the disease was on the hip and leg, and in the remainder one or other part of the upper half of the body was affected: the face, arm, hand, elbow and neck; and in one of these cases the buttock in addition. The duration of the disease varied considerably in the different cases, from 3 months to 36 years. None of the cases had undergone light or X-ray treatment, whereby the character of the bacilli might have been altered. Some had been treated by scraping or curetting, others had not been treated at all.

23. Our investigations of cases of human tuberculosis other than lupus have shown that from internal lesions there was obtainable one or other type of tubercle bacillus, either the bovine tubercle bacillus or the human tubercle bacillus; that, from a few cases only, both bovine bacilli and human tubercle bacilli were obtained. The identification of these bacilli from internal tuberculosis of the human subject was based on certain experimental data: viz., the cultural characters of the bacillus and its pathogenic effects when injected into animals. It is not necessary to repeat here what has already been said on this point. For the present purpose the following considerations may be emphasized: the bovine bacillus on the one hand possesses characteristic cultural features and when subcutaneously injected is highly virulent for the calf and the rabbit in certain defined doses, and for the monkey and guinea-pig in very small doses. On the other hand the human tubercle bacillus grows more luxuriantly on artificial media than the bovine bacillus and when subcutaneously administered is only slightly virulent for the calf and rabbit, but is, like the bovine bacillus, highly virulent for the monkey and guinea-pig in very small doses. These facts need to be borne in mind when considering the results of our investigation of lupus cases. For it has been found that the bacilli isolated from certain cases of lupus exhibit a pathogenicity or degree of virulence differing from that which would have been anticipated from a study of their cultural characters alone. The following table shows the general results obtained:—

Classification of Lupus Viruses according to Cultural Characters and Virulence.

Virus.	Cultural Characters.	Virulence for the Calf, Rabbit, Monkey and Guinea-pig.
(1.) H 110. "J.B." ...	Bovine (Class I.)*	Like the bovine bacillus virulent for the calf, rabbit, monkey and guinea-pig.

* *See* 2nd Interim Report Appendix, Vol. III., page 5.

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* Material from one other case of lupus (H 113. "O.S.") was obtained, but guinea-pigs inoculated with it did not develop tuberculosis. No tubercle bacilli were seen in a smear preparation made from the material.

Classification of Lupus Viruses according to Cultural Characters and Virulence—continued.

Virus.	Cultural Characters.	Virulence for the Calf, Rabbit, Monkey and Guinea-pig.
(2.)		
H 100. “R.S.” ...	Bovine (Class II.)	All these had lower virulence for the calf than the bovine bacillus. In rabbits although generalised tuberculosis was produced the duration of life was longer than with the bovine bacillus. In guinea-pigs and monkeys the disease was less severe than with a similar dose of the bovine bacillus or of the human bacillus.
H 105. “G.S.” ...	Bovine (Class I.)	
H 53 “D.H.” ...	Bovine (Class III.)	
H 107. “H.H.” ...	Bovine (Class II.)	
H 108. “H.R.” ...	Bovine (Class II.)	
H 85. “H.B.” ...	Bovine (Class II.)	
(3.)		
H 111. “S.E.” ...	Bovine (Class III.)	For the calf this had low virulence, not higher than that of the human tubercle bacillus. Intravenously in rabbits fatal tuberculosis was produced; subcutaneously, chronic tuberculosis. Virulence for the monkey and guinea-pig was lower than that of either the bovine or the human tubercle bacillus.
(4.)		
H 91. “H.S.” ...	Bovine (Class III.) Slightly pigmented growth on serum.	This had low virulence for the calf, no greater than that of the human tubercle bacillus, and for the rabbit lower than that of the human tubercle bacillus. For the guinea-pig lower and for the monkey much lower virulence than either the human or bovine tubercle bacillus.
(5.)		
H 99. “L.K.” H 92. “D.N.”	Human	These resembled the human tubercle bacillus in virulence for the calf, rabbit, monkey and guinea-pig.
(6.)		
H 109. “M.W.” H 112. “B.B.” H 71. “L.V.” H 101. “E.G.” H 114. “A.U.”	Human	These resembled the human tubercle bacillus in virulence for the calf and rabbit. They were less virulent for the monkey and guinea-pig than the human bacillus.
(7.)		
H 103. “N.S.” H 106. “K.R.” H 84. “M.S.” H 102. “N.H.”	Human	These had very low virulence for the calf and rabbit, and lower virulence for the monkey and guinea-pig than the human tubercle bacillus. H 102. “N.H.” was the least virulent of all the lupus cultures.

24. The bacilli isolated from these several lupus cases retained their cultural characters after repeated subcultivation and also after residence in the animal body. Numerous cultures were made from lesions in the calves and other animals inoculated and the cultures thus obtained preserved the cultural characters of the bacilli isolated from the original material. Despite this cultural constancy, it is evident from a consideration of the results shown in the Table that only three of the viruses behaved pathogenically like the types of the bacilli (the bovine bacillus and the human bacillus) which are found in the internal lesions of human tuberculosis. These viruses are H 110. “J.B.”, which is identical with the bovine bacillus in cultural characters and in virulence, and H 99. “L.K.” and H 92. “D.N.”, which are

in cultural characters and in virulence identical with the human tubercle bacillus.

25. Of the remaining seventeen lupus viruses we found eight showing the characters of the bovine tubercle bacillus in culture, but differing from the bovine bacillus in their effects when injected into calves and rabbits, monkeys and guinea-pigs. As regards certain of these eight viruses, some of those included in (2) of the Table showed a very wide range in their virulence for the calf. For instance, in the case of virus H 100. "R.S.", one calf (*1523*) developed fatal generalised tuberculosis from a dose of 50 milligrammes; three other calves, one of which (*1419*) received a dose of 50 milligrammes and two (*1409* and *1547*) a dose of 100 milligrammes each, were killed in 95 to 122 days and showed generalised tuberculosis of a not very severe type, progressive in one, retrogressive in the other two. With another virus (H 53 "D.H. b.") fatal generalised tuberculosis followed in 52 and 63 days respectively from a dose of 50 milligrammes in two (*1507* and *1545*) out of three calves; whereas the third calf (*1535*) receiving a similar dose showed slight generalised but retrogressive tuberculosis.

With none of the other of these dysgonic lupus viruses was fatal tuberculosis produced in the calf by doses of from 48 to 96 milligrammes within 90 days. Certain of these animals showed only retrogressive and limited tuberculosis not fatal within the 90 days; while in other calves again there were intermediate effects, *i.e.*, the disease was widespread but not fatal within 90 days. A minimal result was obtained in one calf (*1331*) injected with 96 milligrammes (H 85. "H.B."); the animal killed 90 days after inoculation showed disease limited to the site of inoculation and the nearest gland. Another calf (*1289*) injected with a dose of 50 milligrammes of culture of the same virus showed slight retrogressive generalised tuberculosis in 94 days. Slight effects such as these are not obtained in calves with these doses of the bovine tubercle bacillus when derived from the lesions of bovine tuberculosis, and there can be no question therefore as to the feeble virulence of many of these dysgonic lupus viruses. In this respect the experiments performed on rabbits confirm the results obtained in calves, *i.e.*, as regards the wide and lower range of virulence of the viruses.

Moreover, feeble virulence was especially well seen when certain of these viruses were injected into guinea-pigs and monkeys; for instance, with viruses H 111. "S.E." and H 91. "H.S.", both of which viruses were in culture bovine in character. The first (H 111) had virulence for the calf and for the rabbit lower than that of the bovine and for the calf not higher than that of the human bacillus, but its virulence for the monkey and guinea-pig was less than that of the human bacillus. The second (H 91) had low virulence for the calf and rabbit, *i.e.*, not greater than that of the human bacillus, while for the guinea-pig and monkey it had lower virulence than the human bacillus.

26. In view of the above facts and on a working assumption that the dysgonic tubercle bacilli found in lupus might be degraded bovine bacilli, it was sought to increase their virulence by passage through animals. Certain of the viruses were accordingly thus tested, the tissues of calves and rabbits being regarded as most likely to induce intensification of their virulence. These viruses were the six which are shown in the Table (2). One experiment with Virus H 100. "R.S." may be quoted to illustrate the result obtained. The culture derived from the original material through a guinea-pig was injected subcutaneously into a calf (*1409*) in a dose of 100 milligrammes. The animal was killed in 119 days and only a limited tuberculosis was found: a cyst at the seat of inoculation, a few tuberculous lesions in the nearest glands and in the lungs, and in a few lymphatic glands of the body—a result very different from that which follows inoculation with 100 milligrammes of a culture of bovine tubercle bacilli. A culture obtained from the mediastinal gland of this calf was inoculated into another calf (*1543*) in a dose of 50 milligrammes. This second calf was killed, when dying, in 34 days and showed general miliary tuberculosis. Two other experiments with the same virus on similar lines lasting respectively 73 and 122 days gave like results. The cultures obtained from the passage animals in each series were also fully virulent for rabbits. In another experiment the virulence of Virus H 100 was found increased for the rabbit by residence for 337 days in the body of the rabbit. Apparently, therefore, residences in a calf for 73, 119 and 122 days of the bacilli obtained from the lupus lesion was sufficient to raise the virulence of the bacillus to that of the bovine tubercle bacillus, and residence in the rabbit for 337 days had like effect.

Similar results were obtained with Virus H 108. "H.R."

But in the cases of Viruses H 105. "G.S.", H 53. "D.H.", H 107. "H.H." and H 85. "H.B.", the result was different; neither a single residence in the calf or rabbit, nor passage through a series of calves, led in these cases to an increase of virulence up to the standard of the bovine tubercle bacillus. In one case, however (H 105. "G.S."), the virulence for the rabbit was slightly increased by passage through the calf, and in another (H 53. "D.H.a"), for the monkey by passage through the monkey.

To sum up the results obtained in these nine cases of lupus in which a bacillus was obtained presenting the cultural characters of the bovine tubercle bacillus, in only one case did the bacillus obtained from the original material possess the high virulence as well as the cultural characters of the bovine tubercle bacillus. The other eight viruses, though their bacilli exhibited and retained the cultural characters of the bovine tubercle bacillus, proved less virulent than that bacillus not only for the calf and rabbit but also for the monkey and guinea-pig. It was found possible in two cases to increase the virulence of the culture from the original material by residence in the tissues of the calf and rabbit so as to bring it up to the high virulence of the bovine tubercle bacillus.

27. There remain for consideration eleven lupus viruses the original cultures from which manifested the cultural characters of the human tubercle bacillus. All these showed low virulence for the calf and rabbit, agreeing in this respect with the human type of the bacillus, though some of them exhibited for these animals much less virulence than that bacillus. They differed, too, from the human tubercle bacillus in that generally they had a lower, some of them a much lower (the four viruses in 7 of the Table), virulence for the monkey and guinea-pig.

The effects of the lupus viruses on rhesus monkeys are of especial interest. With the exception of the three (H 110, H 99, and H 92) which produced fatal general tuberculosis in these animals in no wise differing from that set up by human or bovine tubercle bacilli, none of the viruses, 17 in number, was equal in virulence to the human or to the bovine tubercle bacillus. Progressive generalised tuberculosis was, it is true, produced by each of these viruses, but this led to a fatal result only after longer, and in some cases much longer, periods than the tuberculosis caused by the typical bovine or typical human tubercle bacillus. Eight of these 17 viruses had the cultural characters of the bovine tubercle bacillus and nine had those of the human tubercle bacillus. These effects on monkeys supply further evidence that viruses may possess a virulence differing from that which was to have been anticipated from the cultural characters of the bacillus.

It may be noted that the bacillus of one virus, H 84. "M.S.", after residence in a monkey (*145*) for 139 days was found to be increased in virulence, the virulence being then raised to that of the human tubercle bacillus for the monkey and guinea-pig.

SECTION IV.

Swine Tuberculosis.

28. Tuberculosis is not an uncommon disease in swine, and the lesions from 63 individual cases were investigated. Four of these have to be excluded from consideration owing to the fact that cultures were not obtained. There remain 59 cases which were completely examined as regards the type of bacillus isolated from the lesions.

Appendix, Vol. III. p. 145.

In swine the commonest method of infection is by ingestion of tuberculous material, and the parts first affected are the lymphatic glands in close relation to the alimentary tract (submaxillary, pharyngeal, and mesenteric). The abdominal organs, especially the spleen, are not infrequently involved, and in many cases the organs of the thorax as well.

29. The specimens investigated were obtained in all cases from the slaughter-house, and were taken from the carcases of animals sent there for the purpose of being slaughtered for food. It was found impossible to obtain a complete post-mortem record of each pig the lesions of which were used for investigation. In a certain number of the cases the disease was stated to have been localised in the glands of the neck and in certain others it was stated to have been generalised.

In some of the former, the internal organs having been removed before examination of the carcass was made, lesions may possibly have been present elsewhere in the body. The investigation of these local lesions can therefore be held to concern only the disease which had affected the glands in question. In the generalised cases on the other hand, that is where the material was obtained from lesions of the internal organs, the investigation must be considered as dealing with the generalised disease as it occurs in the pig.

In 26 cases the disease was stated to have been localised; in 25 of these the lesions submitted for examination were in the submaxillary glands and in one in the mesenteric glands only. In 33 cases the disease was generalised; in the majority of these it was of moderate severity, although in a few instances there were only scattered lesions throughout the body.

30. The material used in the investigation of the 59 cases was obtained from the following parts:—Submaxillary glands, 44 cases; bronchial glands, 4 cases; spleen, 2 cases; mesenteric glands, 2 cases; submaxillary and bronchial lymphatic glands, 1 case; skin, bone, joint, lung, udder, and inguinal gland, 1 case each. Cultures were obtained direct from the original material in all but four instances; in these four cases they were obtained after the inoculation of the original material into guinea-pigs. In securing cultures in swine tuberculosis it is of importance to obtain them direct from the original material if practicable, for the reason that the pig is capable of harbouring more than one type of tubercle bacillus, and one of the types of bacillus (namely the avian) might escape detection if guinea-pigs were inoculated for the purpose of cultures being grown from the lesions produced in them. In the guinea-pig the avian bacillus does not induce progressive tuberculosis and the lesions produced may be minimal.

The cultures which were obtained from these lesions were observed as to their mode of growth and were used for inoculation into guinea-pigs, rabbits, calves, fowls and other animals in order to determine the characters of the bacilli present, whether bovine, human, avian, or a mixture of these.

31. The results thus obtained are shown in the following table:—

Degree of Tuberculosis in the Pig.	Bovine Virus.	Human Virus.	Avian Virus.	Mixed Avian and Bovine.	—
Local Tuberculosis	18 cases	3 cases	5 cases	—	26
Generalised Tuberculosis ...	32 „	—	—	1 case	33
	50 cases	3 cases	5 cases	1 case	59

From this Table it is evident that all three types of bacillus are capable of infecting the pig—the bovine tubercle bacillus, the human tubercle bacillus, and the avian tubercle bacillus.

32. The cases of infection by the bovine tubercle bacillus were by far the most numerous: 50 cases out of 59. Though in many of these 50 cases the only tuberculous lesion detected at the time of slaughter was in the submaxillary lymphatic glands, in many others of the 50 this bacillus had produced generalised tuberculosis, and in our experience the bovine bacillus only has been found to be the cause of natural generalised tuberculosis in pigs.

The cultures obtained from all these 50 cases were identical in mode of growth with the bovine tubercle bacillus. They were also identical in virulence with the bovine tubercle bacillus, with one exception, Virus P. XIV. The original culture of this virus in doses of 50 milligrammes produced in four calves generalised tuberculosis but the disease was less severe and of longer duration than that set up in this animal by a similar dose of the bovine tubercle bacillus. A culture from one of the inoculated calves when injected into two other calves caused fatal generalised tuberculosis similar to that caused by a like amount of culture of the bovine bacillus.

33. In three cases of local swine tuberculosis, the human tubercle bacillus alone was found. The bacilli isolated from these cases had the cultural characters of the human type and a low degree of virulence for the calf and rabbit. One of these viruses (P. XLI) though it showed, like the other two, a slight degree of virulence for the

calf and rabbit, produced in the pig after subcutaneous inoculation a severe tuberculous pneumonia in three different instances, a result which has not occurred in our experiments from inoculation into pigs of the human bacillus obtained from human tuberculosis. The culture from the last pig of the series was non-virulent for rabbits like the human tubercle bacillus and resembled that bacillus in cultural characters. One of the three viruses (P. IV) produced rather more severe results in calves and rabbits than had usually occurred in our other experiments with the human tubercle bacillus, but the difference was not great.

34. From five cases of local swine tuberculosis a bacillus was obtained, which, in mode of growth and virulence for animals, was identical with the avian bacillus, as described in this Report on page 7.

35. There remains for consideration one case of swine tuberculosis (P. XLII) in which both avian and bovine bacilli were obtained as a mixed culture from the submaxillary lymphatic glands. This occurred in a pig about eight months old, in which the lungs and liver were stated to have been also very slightly affected with tuberculosis. The original culture on serum was bovine in appearance (the avian element growing badly on this medium), and caused in rabbits and guinea-pigs effects like those produced by the bovine bacillus. The avian element in the culture was separated in a pure form by subculture on glycerin agar incubated at 42° C. It produced characteristic effects in fowls and guinea-pigs, and from one of these guinea-pigs a pure culture of the avian bacillus was isolated.

This result is of some importance in connection with the instances of mixed viruses already described in discussing Human Tuberculosis, and it illustrates the difficulty of deciding the nature of the virus in certain cases without special and, it may be, prolonged investigation, as the following considerations show.

When a culture isolated from a tuberculous lesion is found to grow on repeated subcultivation like a bovine tubercle bacillus, it might be concluded that the avian tubercle bacillus is not present. But this conclusion might not be correct, for as the avian tubercle bacillus grows badly on serum it would not be recognisable in a culture on that medium if present only in a small proportion, as in the original culture of Virus P. XLII. Similarly, when the culture isolated grows like the human tubercle bacillus, the eugonic and luxuriant growth of the culture may hide the presence of the bovine or of the avian tubercle bacillus.

Thus it is not always safe to infer from the mere appearance of a culture that a bovine or an avian element is not present in it; in a case of doubt the only means of determining this is to test the virulence of the culture in calves, fowls, and rabbits, or to separate the two elements by one or other of the methods already described.

36. The results of our investigation of Swine Tuberculosis are clear, and may be summarised as follows :—

All three types of tubercle bacilli are capable of infecting the pig, but the human bacillus and the avian bacillus are less frequently found in this animal than the bovine bacillus. The bovine tubercle bacillus, though in many pigs it may have caused no more than a localised lesion in the submaxillary lymphatic glands at the time of slaughtering the animal, nevertheless in many instances produces a severe and generalised disease. One case of mixed infection with bovine and avian tubercle bacilli was met with and a mixed infection with human and bovine tubercle bacilli must be considered possible in the pig, although it was not found in any of the cases investigated by us.

SECTION V.

Equine Tuberculosis.

37. In horses tuberculosis is in most cases primarily an affection of the glands and organs in connection with the alimentary tract, the abdominal organs being chiefly affected. Five cases of equine tuberculosis were investigated (E I to E V). In one there were tuberculous lesions in the mesenteric glands and spleen; in a second case the mesenteric glands alone were affected; in a third case the spleen was the only tuberculous organ; and in two cases the mesenteric glands, spleen and lungs were affected, the disease having become generalised. **Appendix, Vol. IV, p. 5.**

In three cases the material investigated was from the tuberculous mesenteric glands, in one case from the spleen, and in another case from the lungs, spleen, and mesenteric gland.

38. In four cases the material was first injected into guinea-pigs and cultures were obtained from these animals ; in one instance, Virus E V, the culture was obtained direct from the original material. In all cases the cultures obtained grew like those of the bovine tubercle bacillus. Two of the viruses (E II and E III) belonged culturally to Class I of the bovine series, which comprises cultures that grow the least easily ; one (E I) belonged to Class II and two (E IV and E V) belonged to Class III, in that they behaved like the most readily growing bovine bacilli. In all cases the bacilli obtained from the experimental animals retained their cultural characters after prolonged subculturing, and none showed variation in their mode of growth even in prolonged passage experiments such as were carried out with Viruses E II and E IV.

39. The results of the experiments performed in testing the potency of the bacilli of these equine viruses show that notwithstanding the similarity of their cultural behaviour their virulence is not in all cases parallel with that of the bovine bacillus.

The bacilli isolated from Viruses E I, E III, and E V were exactly similar to the bovine tubercle bacillus in their virulence for rabbits and guinea-pigs. Viruses E I and E III were also tested on calves and pigs, and in these animals caused, like the bovine bacillus, a fatal generalised tuberculosis. Virus E V was not tested on pigs and calves, but the acute tuberculosis which was produced by it in rabbits was so definite in type as to suffice for identifying it with the bovine bacillus. Virus E I was also tested on a pony which received 10 milligrammes of culture intravenously. This pony died in 17 days of acute tuberculosis, an effect similar to that which was produced in this way in the horse by the bovine tubercle bacillus. Virus E III, in a dose of 1 milligramme subcutaneously injected, produced acute tuberculosis in a lemur, death occurring in 28 days.

40. Viruses E II and E IV did not behave like the three viruses above mentioned, nor like the bovine tubercle bacillus, when injected into animals ; and they must be considered separately.

Virus E II, which in culture was found to belong to the class of most dysgonic bovine bacilli, was inoculated into seven calves. Two of these calves (*404* and *406*) inoculated subcutaneously with 10 milligrammes of culture, showed when killed in about 90 days only a very slight amount of disease. Five other calves, of which three received 50 milligrammes each, one 20 milligrammes and one 100 milligrammes subcutaneously, remained in good health after their inoculation, and showed, when killed in from 90 to 100 days, only a slight amount of disease which was apparently retrogressive; an effect similar to that produced in calves by the subcutaneous injection of an equal dose of the human tubercle bacillus. This result, namely, that a culture typically bovine in appearance should have uniformly produced only slight disease when injected into calves, is a notable circumstance.

For rabbits Virus E II was only moderately virulent, for although it caused fatal generalised tuberculosis by intravenous and intraperitoneal inoculation, the duration of life was longer and the extent of the disease less than in the case of rabbits inoculated with the bovine tubercle bacillus. After subcutaneous inoculation the amount of disease produced by E II varied very greatly being sometimes acute, but usually chronic.

For monkeys also this virus was less virulent than the bovine bacillus. After subcutaneous inoculation the course of the disease was less acute than after inoculation with the bovine bacillus, but it was invariably fatal in the end. The disease set up by feeding was still more chronic in its course.

Although in pigs and guinea-pigs subcutaneous inoculation of this virus produced in every case fatal generalised tuberculosis, the disease ran a chronic course.

It may be said, therefore, that the virus of E II, although growing like the bovine tubercle bacillus, produced much less severe effects than that bacillus when inoculated into animals, its slighter virulence for the calf being especially well marked.

41. Similar experiments were performed with the virus of E IV. Six calves were inoculated subcutaneously, two with doses of 10 milligrammes, and four with doses of 50 milligrammes. Five of these remained well, and when killed, in about three months, showed slight non-progressive tuberculosis. The sixth calf died in 89 days of a severe tuberculous pneumonia, but with very little disease elsewhere. This result is possibly to be explained on the assumption that the injection was

accidentally intravenous as well as subcutaneous. It is clear that the virus of E IV, like that of E II, was not as virulent for the calf as the bovine tubercle bacillus.

For rabbits this virus was only moderately virulent, the results in that animal being similar to those obtained with the virus of E II.

The baboon and rhesus monkey were less susceptible to this virus than to the bovine bacillus. For example, a baboon (*74*) fed with a dose of 1 milligramme of culture was killed in 448 days when still apparently in good health ; post mortem there was found very slight and non-progressive tuberculosis. The culture obtained from lesions in this animal was unchanged in character as compared with the original culture, and was not increased in virulence for the calf or rabbit.

Virus E IV, like Virus E II, produced generalised tuberculosis in pigs and guinea-pigs. It also produced generalised tuberculosis in horses both by intravenous inoculation (10 milligrammes) and by subcutaneous inoculation (50 milligrammes), while E II produced a similar effect by intravenous inoculation. Both E II and E IV were found non-virulent for fowls.

42. Viruses E II and E IV therefore closely resembled each other in the following points. The bacilli isolated from them, although they had the characters in culture of the bovine tubercle bacillus, differed from that bacillus in that they did not produce an acute disease in calves with doses of 50 milligrammes and more of culture given subcutaneously. Less severe disease too was produced by these two viruses than by the bovine bacillus in rabbits and monkeys ; and though they, like the bovine bacillus, were capable of producing acute disease in pigs and guinea-pigs, these animals survived longer after inoculation with E II and E IV than after inoculation with the bovine tubercle bacillus.

On the whole the properties of these viruses more closely resembled those of bovine tubercle bacilli than those of the other two types of tubercle bacilli—the human and the avian. Accordingly, experiments were undertaken to ascertain whether by passage of culture of the original material of these viruses through calves and, to a less extent, through rabbits and monkeys, their virulence could be enhanced and brought parallel to that of the bovine bacillus.

43. *Passage Experiments with Virus E II.*—Four separate passage experiments on calves were undertaken. (*See* Chart, Appendix, Vol. IV, page 105.) The first passage experiment was through calves, two series of these animals being tested concurrently, and lasted 2½ years. Cultures were used, the dose for the first animal being 10 mgs. while the succeeding calves received 50 mgs. each. As a result of the passage the virulence for the calf was perhaps increased slightly, but for rabbits it was definitely increased.

The second passage experiment was carried out, like the first, through a double series of calves and lasted 2 years and 7 months. In one branch of the experiment the virulence of E II for the calf became increased up to the standard of the bovine bacillus. In the other branch the virulence was not increased.

The third and fourth passage experiments each included 4 calves and lasted 1 year and 4 months and 1 year and 7 months respectively. In both experiments there was an increase of virulence of E II up to the standard of the bovine tubercle bacillus.

In parallel experiments on rabbits performed with each of the cultures isolated during the passage through calves, it was found that the results obtained with the rabbits coincided with those obtained with the calves. The cultures which produced slight tuberculosis in calves had not the virulence for rabbits of the bovine bacillus, whereas those which killed the calves with acute tuberculosis killed the rabbits with acute disease. In one instance the culture obtained from one of the calves which died of generalised tuberculosis was found fully virulent for the monkey, whilst in another instance in which at the end of the passage the calf had only slight tuberculosis the culture obtained from it was found not to be increased in virulence for the monkey. Throughout all the passage experiments the cultural characters of the bacillus remained unaltered. In one experiment a culture derived from a rabbit which had been inoculated with a culture from the original material of E II was found to have increased virulence for the calf, in which it produced severe generalised tuberculosis.

44. *Passage Experiments with Virus E IV.*—Three passage experiments were performed, two of which were negative and one positive. (*See* Chart, Appendix, Vol. IV, page 123.) The first passage lasted 2 years and 4 months and began with a dose of 10 mgs. injected subcutaneously into a calf. A culture

from this calf, passed on in doses of 50 mgs. into other two calves, produced only slight disease. Cultures from each of these two calves passed on in a similar dose into each of two other calves also produced but slight disease.

The second passage experiment lasted 1 year and 7 months : a dose of 50 mgs. was injected in the first instance and the experiment was performed in the same way and with the same number of calves as before ; it was also negative.

The third E IV passage experiment lasted 1 year and 7½ months, and began with a calf (*502*) which received 50 milligrammes subcutaneously ; only slight disseminated tuberculosis was produced in this animal. The culture isolated from the lung of this calf was passed on into two calves (*630* and *614*) in similar doses. One died in 31 days of generalised tuberculosis, the other in 33 days of pneumonia with some tuberculous lesions. Another calf (*602*) inoculated with a culture from the suprarenal body of Calf *502* was killed in 90 days, and showed progressive but not severe generalised tuberculosis. The culture from this calf, injected in a 50 milligramme dose into another calf, killed the animal in 39 days of generalised tuberculosis. The virulence of E IV for the monkey was also increased at the end of the passage.

SECTION VI.

Cases of Natural Tuberculosis in Mammals other than Man, Ox, Pig, and Horse.

Appendix, Vol. IV, p. 150.

45. From time to time during the course of our investigation opportunity occurred for examining some cases of natural tuberculosis in mammals other than man, the ox, the horse, and the pig. Five such cases were studied in the following animals : a gnu, an antelope, a rhesus monkey, a chimpanzee, and a cat.

46. The gnu (*connochœtes taurinus*) died at the Zoological Gardens from generalised tuberculosis, the parts affected being the lungs, liver, and a few glands in the thorax and abdomen. Cultures were obtained direct from the lung, a mediastinal gland, and a portal gland. The bacillus from each of these parts showed in culture the characters of the human tubercle bacillus. One of these cultures was tested on calves and rabbits, and was found to produce the same effects as the human tubercle bacillus.

47. The antelope (*oryx beisa*) was killed when ill at the Zoological Gardens, where it had been in captivity for many years. There was extensive tuberculosis, with cavities in the lungs, which were the parts used for investigation. Cultures were obtained direct from the lung, and showed the characters of the human tubercle bacillus. The virulence of these cultures was tested on calves, pigs, and rabbits, as well as on guinea-pigs. In the three former animals it produced only localised disease similar to that caused by the human tubercle bacillus. A series of passage experiments was performed on rabbits. There was no evidence of the presence in the virus of the bovine tubercle bacillus, nor was the original virulence of the bacillus altered by the passage.

The presence of the human tubercle bacillus in these two animals, the gnu and the antelope, and the fact that they suffered from severe tuberculosis is of some interest as both these animals are ruminants. The human tubercle bacillus has not been isolated by us from any case of natural tuberculosis in a bovine animal.

48. The rhesus monkey was killed at the quarantine station at Isleworth on account of illness and was found to have tuberculosis of the lungs, bronchial glands, spleen, liver and kidney, the disease not being very extensive in any part except the lungs. A culture isolated from the lung grew like the human tubercle bacillus and had only slight virulence for rabbits.

49. A chimpanzee which had been purchased by the Commission as apparently a healthy animal died shortly afterwards during its period of quarantine at Isleworth of acute miliary tuberculosis, starting from the intestinal tract. A culture isolated from its mesenteric gland grew like the human tubercle bacillus and behaved like this bacillus when inoculated into rabbits and guinea-pigs.

In all the four cases described above the human tubercle bacillus was the cause of the naturally acquired disease.

50. The mesenteric gland of a cat suffering from naturally acquired tuberculosis was investigated. The culture isolated direct from the gland grew like the bovine tubercle bacillus (Class II). Like this bacillus it produced fatal generalised tuberculosis in rabbits.

The only comment which it is necessary to make on these cases is that the tuberculosis developed by mammals kept in captivity may be due either to the human tubercle bacillus or to the bovine tubercle bacillus. Owing to the small number of cases investigated, no conclusions can be drawn as to the relative frequency of infection of such animals by the one or the other type of bacillus.

SECTION VII.

Avian Tuberculosis.

51. The characters and properties of the avian tubercle bacillus have already been discussed by us on pages 7 and 8 of this Report. There remain to be noted our observations of avian tuberculosis as it occurs naturally in birds and pigs. Appendix, Vol. IV, p. 167.

The cases of tuberculosis in birds which were investigated by us occurred in three fowls, three pheasants, a pigeon, a demoiselle crane, and a Senegal touracou*. In these cases the disease revealed by the post-mortem examination showed the well known features of tuberculosis in birds, viz., the presence of tuberculous nodules in the intestine, spleen, and liver. In some cases the lungs, joints, and bones were affected.

52. The material used for investigation in the different cases was : the spleen, four cases ; spleen and liver, one case ; liver, one case ; lung, two cases, and an intestinal nodule, one case. Cultures were obtained from the original material directly except in one case in which the culture was obtained from a rabbit which had been inoculated with the lesions of a fowl.

In all cases the bacilli isolated proved to be identical with and had the characters and properties of the avian tubercle bacillus as already described.

The avian bacillus was also found in the submaxillary lymphatic glands in six cases of tuberculosis in pigs ; in five alone and in the sixth case in association with the bovine tubercle bacillus (page 21).

SECTION VIII.

Behaviour of Bacilli and Fate of Bacilli in the Tissues of Animals Inoculated and Lesions Produced.

53. During the course of our investigation concerning the virulence of the three types of tubercle bacilli in various animals numerous observations were made on the inter-action of the bacilli and the tissues of the inoculated animals as regards the distribution of the bacilli, their fate in the tissues and the lesions produced by them.

These observations were made by the investigators conducting the experiments, Drs. Cobbett, A. Stanley Griffith and F. Griffith ; the histological and some of the bacteriological observations being made by Dr. Arthur Eastwood. The results of these observations, which will now be discussed, have an important bearing on the relation of the three types of bacilli to each other, in that they enable comparison to be made of the effects in animals of each of the several types. Moreover, the results of the observations on the lesions produced by the different methods of inoculation and by feeding, and on the sequence of the lesions, have a bearing on the question of the seat of primary tuberculosis as it occurs in man and animals.

54. In previous sections of this Report the results of introducing each of the three types of bacilli into various animals have been discussed without entering into any detail as to the histology of the lesions produced, or as to the fate of the bacilli in cases where no lesions resulted. The successful infection of an animal with tuberculosis usually leads to the formation of well-defined lesions which have a definite anatomical structure and undergo certain changes. In some cases the disease rapidly involves numerous parts of the body ; this we call acute or miliary tuberculosis. In other cases, though not so acute, the disease is progressive and consists in the gradual formation and development of lesions in various organs, but some of such cases may become retrogressive. In

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* We have not investigated cases of natural tuberculosis in parrots, but we are aware that other observers have isolated the human tubercle bacillus from the lesions occurring in such cases.

other cases the disease remains localised at the site of inoculation without any apparent effect on the general health of the animal, and such cases may end in complete recovery. We have recognised, however, that other events may happen when tubercle bacilli are introduced into the animal body. In some cases the bacilli die and disappear without leaving any lesions ; in other cases the bacilli become dispersed throughout the body where they may even multiply, sometimes to an enormous extent, but without producing any lesion.

55. In our Second Interim Report we recorded experiments performed by Dr. Cobbett, Dr. A. Stanley Griffith and Dr. F. Griffith, in which the distribution of bacilli in the animal body was investigated at an early date after their introduction beneath the skin. Other experiments have since been performed by Dr. A. Stanley Griffith on the same subject.

2nd Int. Rep., Appendix, Vol. III, p. 219.

Experiments on calves with the human tubercle bacillus by Dr. Cobbett (Viruses H 46 and H 26) showed that after subcutaneous injection of the calf with a dose of 50 milligrammes of culture tubercle bacilli could be demonstrated, by means of inoculation of the calf tissues into guinea-pigs, after 25 days in the liver, lung, spleen and rib marrow of one calf, and that in another calf, after a lapse of 90 days from the injection, the lung was found (by like means) to contain tubercle bacilli, though these were absent from the spleen, liver and rib-marrow. In neither of these cases were there visible tuberculous lesions in the organs of the calf. In another experiment on a calf the human tubercle bacillus was subcutaneously injected in a dose of 50 milligrammes of culture. This animal was killed in three days and the presence of tubercle bacilli in the spleen, liver and lung, bone marrow and popliteal gland was detected by the production of tuberculosis which followed the injection of an emulsion of these parts into guinea-pigs. A similar result was obtained eight days after subcutaneous injection in another calf and after 14 days in a third calf; after three months in a fourth calf tubercle bacilli were still present in the lungs, liver and spleen. After three months in a fifth calf also the results were positive in the lung, the popliteal gland, the thoracic, bronchial and hepatic glands, but the other organs were free from tubercle bacilli. In Dr. Cobbett's words, " Tubercle bacilli are frequently present in the organs and glands of bovine animals several months after they have been injected subcutaneously with human tubercle bacilli." It is clear indeed that in the early stages of invasion these bacilli produce no visible lesions in the organs, but that after some months their presence may result in the formation of minute fibrous or calcareous tubercles which are non-progressive. Such lesions have been found on post-mortem examination in about 50 per cent. of the calves injected subcutaneously with large doses of the human tubercle bacillus.

2nd Int. Rep., Appendix, Vol. III, p. 235.

Dr. A. Stanley Griffith and Dr. F. Griffith, investigating the same subject, employed a variety of animals: the calf, monkey, pig, cat, rabbit, guinea-pig, rat and fowl. Cultures of the bovine bacillus were injected by them subcutaneously into a monkey (20 milligrammes), a calf (44 milligrammes), and five pigs (each 20 milligrammes), two rats (each 10 milligrammes), one fowl (10 milligrammes), one guinea-pig (10 milligrammes), and one rabbit (10 milligrammes). Cultures of the human tubercle bacillus were injected subcutaneously into a cat (10 milligrammes), two rabbits (20 and 10 milligrammes), one pig (20 milligrammes), and two guinea-pigs (10 milligrammes). Most of the above animals were killed in 24 and 48 hours ; the remainder, four pigs, in 3, 5, 8 and 14 days respectively. It was found that in all cases, that is both with the bovine tubercle bacillus and the human tubercle bacillus, there was evidence of dissemination when the animals were killed ; the bacilli being found in the blood, lungs, and the other organs of the body. Bacilli were present in the blood even when the human tubercle bacillus was used for injection.

From the above experiments it is obvious that after subcutaneous inoculation rapid and abundant distribution of bacilli over the body takes place, provided the infective dose has been large and the tissue conditions of the animal such as to allow it to take full effect. Essentially this is a mechanical dispersion, by means of the blood vessels and lymph channels, of a considerable proportion of the injected bacilli occurring speedily on their insertion into the body ; and the acute tuberculosis resulting from such doses of virulent tubercle bacilli is in its inception in strong contrast to the similar but more slowly developing generalised disease induced by smaller experimental doses or such as occurs, it would seem, most commonly in nature.

This more slowly developing, though acute, tuberculosis is due also to dispersion of bacilli by means of blood vessels and lymphatics, but the bacilli thus dispersed are not necessarily those primarily invading the animal : rather they are their progeny which, protracted conflict between invading bacteria and resisting tissue of the local lesion having been decided in favour of the invaders, have multiplied greatly at the site of primary infection. Both these possible processes of invasion are to be taken into account in considering the method of infection that has probably operated in any case of naturally occurring tuberculosis.

In the case of speedy dispersion of a multitude of inoculated bacilli such as no doubt occurred in the experiments above referred to, the result to the animal, if the bacilli are virulent, is that they produce almost at once and in many different parts of the body lesions of greater or less size, no doubt in proportion to the number of bacilli present. This occurs with the bovine bacillus. In the case of the human bacillus, injected, say, into a resistant animal like the calf, although the bacilli are distributed like the bovine bacillus, they do not produce progressive lesions, though they may induce the indolent, non-progressive tuberculous foci seen in the internal organs of so many of the calves subcutaneously inoculated with the human bacillus.

56. It is important in this matter of distribution and fate of tubercle bacilli in the tissues of the invaded animal, to compare with results such as follow subcutaneous inoculation, the effects obtained by administration of tubercle bacilli along with food ; the latter process of experimental infection having been adopted by us as most nearly parallel with conditions under which in nature a large amount of tuberculous infective material may get opportunity of suddenly invading the animal body. In our Second Interim Report feeding experiments with large doses of the bovine bacillus administered to dogs and pigs were recorded, and it was shown conclusively that after ingestion the bovine bacillus can pass through the mucous membrane of the intestine within a comparatively short space of time, and become lodged in the adjoining lymphatic glands.

2nd Int. Rep., Appendix, Vol. I, pp. 499–706.

Further study of the subject has been made by Dr. A. Stanley Griffith in the pig, goat and cat. Two pigs were fed with large doses of bovine tubercle bacilli and seven with similar doses of human tubercle bacilli. In the case of the two pigs fed with the bovine bacillus, the presence of bacilli was demonstrated, by means of inoculation into guinea-pigs, in the submaxillary and mesenteric glands and lungs in seven and thirteen days after the ingestion of the bacillus, but not in the other organs of the body. In five of the seven pigs fed with human tubercle bacilli in from two to twelve days these bacilli were present in the mesenteric and submaxillary glands alone, while in the other two pigs they were present in the lungs as well. In a goat the human tubercle bacillus after ingestion was found in eight days in the submaxillary glands, mesenteric glands and lung ; and in a cat, fed with the same bacillus, bacilli were found in nine days in the submaxillary and mesenteric glands, lung, liver and spleen. Three rhesus monkeys were fed each with 50 milligrammes of human tubercle bacilli ; one killed in two days showed no bacilli in the glands or internal organs ; the second killed in four days showed bacilli in the mesenteric glands, liver, spleen, and lungs ; while the third killed in six days showed bacilli in the submaxillary and mesenteric glands and spleen, the experiment with the lungs failing, owing to premature death of the guinea-pigs.

Appendix, Vol. I, pp. 48–52.

After ingestion the distribution in the organs of the body, therefore, of the bovine and human tubercle bacillus is much slower than after subcutaneous inoculation. In these experiments the bacilli which had passed through the mucous membrane of the intestine were arrested in the adjacent glands ; some, however, appeared to have passed into the lungs and other organs of the body.

57. Certain experiments which were performed by Dr. A. Stanley Griffith in investigation of the question as to excretion of the tubercle bacilli into the milk of healthy cows and goats after subcutaneous or intravenous inoculation of these animals with cultures deserve mention. A large dose (100 milligrammes) of bovine culture was injected subcutaneously into a healthy milch cow (Cow *300*), with the result that her milk caused tuberculosis in guinea-pigs by the end of the first week and on every subsequent occasion. This cow died in thirty days of general tuberculosis but her udder was normal both to the naked eye and on microscopical examination. In two other experiments on cows with the human tubercle bacillus it was shown not only that these tubercle bacilli, when subcutaneously inoculated, were excreted in the cow's milk, but that in some cases the excretion of them lasted

Appendix, Vol. III, p. 81.

for a considerable time, and in addition there was evidence of some multiplication of tubercle bacilli in the milk sinuses. In one cow (Cow *77*) which received 100 milligrammes of culture of the human tubercle bacillus subcutaneously, tubercle bacilli were present in her milk 24 hours later, and the milk, in small doses, also caused tuberculosis in guinea-pigs 155 days later as well as at intermediate periods, the udder being found normal when the cow was eventually killed. Of one cow (Cow *565*) which received 10 milligrammes of similar culture intravenously the milk was found to contain these tubercle bacilli 24 hours after inoculation and up to 14 days, but not subsequently. This cow was killed in 182 days and showed no tuberculous lesions. Similar experiments performed on milch goats (six in number), with both bovine and human tubercle bacilli, were confirmatory of the results obtained in cows. It would appear, therefore, from the results of these experiments that the inoculation of large doses, whether of bovine or of human tubercle bacilli, may result in the excretion of tubercle bacilli in the milk of the cow and of the goat without any disease of the udder being produced, and that in the case of the human tubercle bacillus, these bacilli may, when large doses are employed, be present in their milk for a long time after inoculation.

Appendix, Vol. III, p. 94.

58. Other experiments were performed to determine whether after subcutaneous inoculation of large doses of culture tubercle bacilli could be found in the undeveloped udders of heifers, 6–18 months old. Of the 12 experiments performed, two were carried out with human tubercle bacilli in doses of 68 and 100 milligrammes, eight with lupus viruses in doses of 50 to 100 milligrammes, and two with the bovine tubercle bacillus, the doses being emulsion estimated to contain 4½ million tubercle bacilli and 50 milligrammes of culture respectively. The heifers were killed in 62 to 127 days and in all but four of them tubercle bacilli were found in the milk sinuses of the undeveloped udder; in four cases they were present in such numbers as to suggest that they had multiplied in these sinuses.

59. We proceed now to consider the formation of tuberculous lesions which have been produced in different animals by the injection of each of the three types of bacilli. It is true that in some animals the intravenous inoculation of any one of the three types of bacilli will, in an appropriate dose, lead to the death of the animal. But in some of these cases such inoculation does not, as has been said, lead to the formation of tuberculous lesions in the organs of the body, and the condition produced is so acute as not to afford a correct idea of the pathological process usually occurring in the spread of tuberculosis in the animal body. More clearly interpretable results are obtained when bacilli are inoculated subcutaneously or intraperitoneally, or when administered by feeding.

Tuberculosis is a disease produced by the tubercle bacillus and characterized by the formation of definite lesions or tubercles. These lesions are a manifestation of the resistance of the body to invasion by the bacillus. Histologically, the tuberculous lesion is composed of leucocytes, "plasma" and other cells, of some tissue elements and of fibrin. The lesion varies somewhat in structure, and as the disease progresses it tends to undergo caseation and in some cases calcification.

A chronic lesion is characterised by the formation of a fibrous capsule round the lesion, by the limitation or absence of caseation, or by the extension of calcification.

Appendix, Vol. V.

2nd Int. Rep., Appendix, Vol. IV.

60. It may be said as a result of the work of Dr. Arthur Eastwood that there is no essential difference in the structure of the tuberculous lesion produced experimentally in animals by the bovine tubercle bacillus and the human tubercle bacillus. Lesions that are produced by the avian tubercle bacillus are generally distinguishable from those caused by mammalian tubercle bacilli, but in the case of lesions of a chronic type it may be impossible to decide by microscopic examination alone whether the tubercles were caused by avian or by mammalian bacilli. Accordingly, a comparison of the general results obtained with the three types of bacilli can only be made by considering, in addition to the histological details of the lesions, (1) the comparative effects in different animals as regards the lesions produced and their distribution, progress and extent, and (2) to a less degree the cultural characters of the type of bacillus involved. But it cannot be too clearly laid down that it is the diverse effect in different animals which constitutes the chief difference between the three types of bacilli.

61. The tubercle bacillus may, as has been said, be present in the tissues of certain animals without producing marked or characteristic lesions. An example of this occurs when the bovine or the human tubercle bacillus is introduced into the body of the rat or mouse. Under certain conditions, in

these resistant animals, the bacillus is present in large numbers in the organs, and even in the blood, without forming tuberculous lesions, although there is no doubt from the large number of bacilli found present that they have actually multiplied in the body. In some of the bovine animals injected with the bovine tubercle bacillus, Dr. Eastwood found, in addition to the lesions of the disease, that the bacilli were present in large numbers in some of the tissues without the formation there of lesions, so that this notable multiplication of bacilli in the tissues of the rat and mouse is only, so to speak, parallel with what may occur in animals which show a progressive tuberculosis. With the avian bacillus this condition, viz., the presence of bacilli in the tissues without the production of definitely tuberculous lesions, is perhaps more frequently observed after intravenous inoculation. In the acute infection produced in fowls by intravenous injection of the avian bacillus, the bacilli are present in enormous numbers in the tissues, and even in the blood stream, although no tuberculous lesions are found after death. In monkeys, rabbits and calves the intravenous injection of the avian bacillus may lead to great multiplication of the bacilli in the body without the formation of lesions characteristic of tuberculosis, and similar results may be produced in swine after subcutaneous and intraperitoneal inoculation of this bacillus, and to a less extent after feeding. In goats and ponies intravenous injection of avian bacilli leads to great multiplication of this bacillus, and in the cat and rat injected intraperitoneally these bacilli become disseminated and multiply and survive for a long period with very little tubercle formation. These results are of interest as showing that in the case of highly resistant animals tubercle bacilli even when introduced in large numbers, though producing none but temporary and minimal tuberculous lesions, may multiply in the body of the animal and persist there for a long period. This result is not always obtained, however, for in certain of our experiments mammalian tubercle bacilli, when introduced intravenously, produced but little effect on the resistant animal and soon died.

SECTION IX.

Question of Modification of Bacilli.

62. In Section I of this Report we have set out the special characters of the tubercle bacilli commonly found in bovine animals, man, and birds, and for convenience in describing the results of our investigations we have termed them respectively the bovine, the human, and the avian type of tubercle bacillus. The three types are to be distinguished from each other by their cultural characters and by the effects of their inoculation into various animals. Distinction cannot accurately be made between these types on the basis of microscopic character alone. Morphologically mammalian tubercle bacilli from whatever source derived, are uniform in character when grown on serum. The microscopical characters of mammalian bacilli were described in our Second Interim Report, pages 25 and 26.

Avian tubercle bacilli when grown on glycerin-serum are generally very short ($\cdot 5$ to 1μ) and rather thick, often looking like cocci. Other media commonly yield longer and more irregular forms; and such forms are also sometimes found on glycerin-serum. Amongst these irregularities is found every counterpart to the irregularities observed amongst mammalian bacilli; and, in addition, large club-shaped thickenings are common and branching occurs more frequently than with the mammalian bacillus. In films obtained from emulsions of cultures it is noticeable that avian bacilli are generally distributed; they do not present the solid clumps of closely adherent bacilli which are characteristic of mammalian tubercle bacilli. When growing freely in the tissues the avian bacillus is short, straight, and uniformly stained; when growing under difficulties it is longer and more irregularly stained and is indistinguishable from mammalian bacilli growing under similar adverse conditions.

Appendix, Vol. V, p. 286, and Plate XVI.

63. To the difficult question of fixity of type of bovine, of human and of avian bacilli, we have given much time and attention. There is here involved a problem of much complexity, the facts bearing on it being not only voluminous but in certain senses conflicting, and we have had to regard the problem broadly from two points of view.

First we have had to inquire:—

Whether *as regards naturally acquired tuberculosis* evidence is forthcoming of modification, in any sense great or small, in the ordinary animal body, of any particular type of tubercle bacillus—bovine, human or avian?

And *secondly* we have had to ask ourselves whether *under experimental conditions* any, and, if so what, modification can be induced, and in this connection we have experimented as follows:—

We have—

(*a*) Submitted the several types of bacillus to a series of cultural processes;

(*b*) Submitted them to long sustained influence of the living tissues of the animal body.

Before proceeding to discuss matters from these points of view it is necessary to restate certain considerations which it is essential should be borne in mind in dealing with the question of fixity of type.

64. We have already noted that by the application of appropriate tests three types of bacilli can be recognised, these tests being an examination of the cultural characters of the bacillus on various media, together with a study of the results of its injection into animals. We have shown in our Second Interim Report that the bacilli cultivated from natural cases of bovine tuberculosis and called the bovine type of tubercle bacillus are not absolutely uniform in cultural characters. As compared with the bacilli of the human type they all grow with difficulty upon artificial media, *i.e.*, they are dysgonic. Bovine bacilli from different bovine cases of tuberculosis exhibit diversities in their degree of growth, diversities that are, however, mostly constant; that is, a given bacillus when subcultured for many generations commonly affords in the final cultures a type of growth precisely similar to that which it exhibited when isolated from the original material.

The human type of tubercle bacillus grows more luxuriantly than any bovine bacillus, and this luxuriance of growth has been maintained on repeated subculture and even after passage through animals.

The avian type differs from the other two types in forming a slimy whitish growth which is easily emulsified, and it maintains these characters after repeated subculture.

65. All important in the present connection is consideration of the types of bacilli found in the cases of natural tuberculosis which we have investigated. From all the cases of bovine tuberculosis only one type of bacillus was isolated by us: the bovine type of tubercle bacillus. From all birds suffering from natural avian tuberculosis we have only isolated one form of bacillus: the avian type of tubercle bacillus. From the cases of natural tuberculosis in human beings, other than lupus, bacilli of two types were isolated, the bovine tubercle bacillus and the human tubercle bacillus, and in a few of the cases both types were obtained from the same individual. From pigs, bacilli of all three types have been isolated from natural lesions, the bovine, the human, and the avian. And from certain other animals sometimes the human and sometimes the bovine tubercle bacillus was isolated (Section VI).

Our investigation of cases of lupus, as of human tuberculosis affecting other tissues than the skin, resulted in the isolation of bacilli which culturally were either of the bovine type or of the human type. But in most cases of lupus the bacilli isolated did not correspond in pathogenic effects with the bovine, human, or avian type, and from tuberculosis naturally occurring in horses some of the bacilli isolated also did not correspond in pathogenic effects with any of these three types of bacilli.

66. In most of the cases of natural tuberculosis in mammals investigated by us, the lesions were proved to contain only bacilli which could be definitely referred to either the bovine or human type, this statement being based upon a study of the bacillus by repeated subculturing, and a study of the effect of the bacillus on a series of animals. Wherefore the exceptional results obtained in the cases of lupus and in the cases of equine tuberculosis come to be of great importance in that they demonstrate the occurrence in natural tuberculosis of bacilli which depart widely from the types of bacillus which have been described. These results, therefore, demand restatement.

Appendix, Vol. II, p. 28. There were isolated from six lupus cases bacilli which, although they had the cultural characters of the bovine tubercle bacillus and retained these characters throughout the subsequent investigation, showed a lower virulence for the calf, rabbit, monkey and guinea-pig than the bovine bacillus, and in the case of the two last animals, lower virulence than that of the human bacillus. From two other lupus cases cultures were obtained like those of the bovine bacillus but which were of even lower virulence for the animals mentioned (Section III). In nine other cases of lupus the bacillus isolated had the cultural characters of the human type but was remarkable in that it showed lower virulence for the monkey and guinea-pig than the human bacillus. The cultures obtained in these 17 cases were not mixtures of different types of tubercle bacilli. The repeated investigation of the cultures from each case and the results of their injection into animals showed this. Here, however, we have eight cases in which the culture was bovine in character but had a virulence for animals below that of the bovine bacillus, and nine cases in which the culture was human in character but had virulence below that of the human type of bacillus. These facts are very striking inasmuch as no such divergencies from the recognized types were encountered among the numerous strains of bovine tubercle bacilli isolated from bovine tuberculosis or among human tubercle bacilli isolated from internal human tuberculosis.

Appendix, Vol. IV, p. 7.

67. In the case of equine tuberculosis (Section V) the bacilli isolated from two horses, although growing like the bovine tubercle bacillus, did not in animals behave like that bacillus, in that they were proved by inoculation to be much less virulent for the calf and other animals (guinea-pig, rabbit and monkey). Here again there is a conspicuous divergence from the three types of bacilli previously recognized, the results being similar to those produced by certain dysgonic lupus bacilli.

68. The question accordingly arises: Whether we are to regard these bacilli isolated from cases of lupus and of equine tuberculosis which present exceptional characters and vary, some of them widely, from the three types of bacilli described, as (1) independent fixed types, or (2) modifications on the one hand of the bovine tubercle bacillus and, on the other, of the human tubercle bacillus.

Appendix, Vol. II, pp. 21 & 22.

As bearing on this question the results of experiments with some of the lupus viruses and with two equine viruses must be again referred to (*see* pages 16 and 21). As regards the cases of lupus yielding bacilli which, culturally, were of the bovine type but which did not correspond pathogenically with the bovine type when injected into animals, if it proved possible by experiment to increase the virulence of these bacilli to that of the bovine type, such bacilli might be considered as modified forms of the bovine type. In two cases (H. 100. “R.S.” and H. 108. “H.R.”) it was found that after the lupus culture had been injected into a calf, and carried on from this calf into a second calf it exhibited a virulence fully equal to that of a bacillus of bovine type. A similar result, however, in the calf was not obtained with four of the viruses (H. 105. “G.S.”, H. 53. “D.H.”, H. 107. “H.H.”, and H. 85. “H.B.”). In one of these (H. 105. “G.S.”) the virulence for rabbits was, however, slightly increased by passage through the calf, and in another, (H. 53. “D.H.a”) for the monkey by passage through the monkey. In one of the cases of lupus in which the bacillus isolated had the cultural characters of the human type but a feeble virulence for the monkey, it was found that by a single residence in the monkey for 139 days its virulence was increased to that of the human tubercle bacillus. In other instances the results of the passage were negative.

Appendix, Vol. IV, p. 8.

With the two equine viruses (p. 23) the passage experiments resulted in an increase of virulence of the bacillus up to that of the bovine type.

It can hardly be contended that the cases of lupus in which bacilli with these special characters were found had no etiological connection with ordinary cases of human or bovine tuberculosis, or even with the other cases of lupus in which the bacilli present were of the usual bovine or human type. The virulence of the bacilli in these exceptional cases showed a great divergence from the bovine and from the human type, and if it were to be held that virulence is a fixed quality it would be necessary, in order to classify the lupus viruses, to recognize several new types of tubercle bacilli amongst those which grew like the bovine bacillus but differed from this bacillus in virulence, and several new types amongst those which grew like the human bacillus and differed from it in the same way in virulence. If the proposition were entertained that lupus bacilli are all different types of bacilli, each of which is stable when cultivated and when injected into animals, it would follow that infection in these cases of lupus could not be thought of as having been brought about by tubercle bacilli from cases of ordinary tuberculosis in man or animals; that instead, each of the lupus patients had been infected from an antecedent like case of lupus or by some acid-fast saprophyte resembling the tubercle bacillus. Clearly this proposition is one which cannot be accepted; the less so since by experiments performed with the lupus and equine viruses it has been found possible in some of the cases to enable the bacillus to acquire the full virulence of the bovine tubercle bacillus by residence in the animal body.

The results of our investigation of lupus do not induce us to add a plurality of new types of tubercle bacilli to the three already described. Further investigation of natural tuberculosis in man and animals may possibly disclose other additional variations in the types of bacilli; since not only in human tuberculosis does this disease when affecting the skin furnish types diverging from the human and from the bovine tubercle bacillus, but the internal organs of the tuberculous horse likewise yield divergent types.

69. We pass now to the consideration of artificial conditions specially contrived for inducing modification of type.

We have already stated that we have failed to modify by means of artificial cultivation the pathogenic properties of any one of the three types of bacillus, though for this purpose we have employed many and various media on some of which the bacilli grow more and on others less readily.

We have also investigated the question as to whether by experiment an example of a given type of tubercle bacillus can be modified by prolonged relation with the tissues of the animal body, either during continuous residence in a single animal or repeated passage through a succession of animals. The animals used have been as a rule such as were specially resistant to the growth of the given bacillus, it being considered that in this way modification of type was the more likely to be obtained. It will be borne in mind that in our Second Interim Report we published the results of experiments with human viruses which were relegated by us to a provisional Group—Group III. In certain of those experiments the virus, growing originally like a human tubercle bacillus, was at the end of passage through calves found to be virulent for this animal and to present the cultural characters of the bovine tubercle bacillus. We came to no definite conclusion as regards the explanation of these facts at that time; but in this Report (page 14), as a result of our further investigation, we have shown that these Group III results were due, certainly in most if not in all cases, to the presence of two types of bacilli, the human and the bovine, in the original material, and that during the course of the passage the human type, not developing in the calf, had died out, leaving the bovine type which multiplied and exerted its virulence on that animal. Appendix, Vol. III, p. 5.

70. In further experiments with other viruses designed to effect modification of the type of bacillus, whether human or bovine, we satisfied ourselves that the material used in those experiments contained only one type of bacillus.

In one group of experiments, the investigation was carried out by means of collodion capsules, containing cultures of mammalian tubercle bacilli, which were inserted in the peritoneal cavities of birds.

Appendix, Vol. IV, p. 388. With 10 mammalian viruses, from various sources, 8 of which were bovine, 16 collodion capsule experiments on fowls and 20 on pigeons were performed, lasting from 55 to 186 days. In certain of the cases cultures which were obtained from the capsules on removal from the bird's peritoneal cavity, were placed, again in capsules, in the peritoneal cavities of other birds, the total duration of residence being in one series as much as 475 days. In 20 of these experiments cultures were obtained from the capsules and found to be unchanged in character. In 16 cases no culture could be obtained, the bacilli in the capsules being apparently dead.

Appendix, Vol. I, p. 59. Similar experiments were performed with human tubercle bacilli, obtained from 12 different sources. In nine cases there was only a single residence in the peritoneal cavity of the fowl or pigeon; in three cases the capsules were transferred in series to other fowls. These experiments lasted from 59 to 685 days. In many of the capsules the bacilli were dead, but in the others, the bacilli were alive and showed no change in cultural characters or in virulence.

Appendix, Vol. IV, p. 388. With cultures of five avian viruses 25 collodion capsule experiments were performed on guinea-pigs. The duration of residence in individual guinea-pigs ranged up to 253 days and the total periods during which the cultures were in the peritoneal cavities of series of guinea-pigs varied up to 424 days. In two instances only was there failure to obtain growth of culture from the capsules; from all the other capsules cultures were obtained and were found to be unchanged.

Appendix, Vol. IV, p. 389. As regards further experiments with bovine tubercle bacilli directly introduced into the tissues, two passage experiments on fowls with Virus B. XXVI deserve mention. One of these lasted 2½ years, and included a long series of birds, but no change in the characters of the bacillus was observed. The second lasted the same time with a like result. One of the fowls in the first passage (one of four inoculated at the same time) showed, when killed, avian tuberculosis which was regarded as naturally contracted. It was the only fowl in the two series which was so affected, but this occurrence during the passage shows the danger of drawing conclusions from the result of experiments on fowls unless they are sufficiently controlled.

Among experiments with bovine tubercle bacilli, some on dogs, both by inoculation and by feeding, were recorded in our Second Interim Report. In two of the dogs referred to in that Report residence in this animal appeared to have altered the bovine tubercle bacillus, inasmuch as cultures obtained from these two animals resembled the human tubercle bacillus. In the remainder of the experiments on dogs no change in the bovine tubercle bacillus occurred. In certain further experiments eight dogs were fed with doses varying from 40 to 100 milligrammes of culture of bovine tubercle bacilli and were killed in from 103 to 302 days. From five it was impracticable to secure cultures, but from the remaining animals cultures were obtained which were not changed either in character or virulence. From nine other dogs which had been inoculated by various methods eight cultures were obtained which showed no alteration.

2nd Int. Rep., Appendix, Vol. III, p. 91.

Appendix, Vol. IV, p. 389.

A chimpanzee passage experiment was performed, five chimpanzees being used in series; three of the animals were fed and two were inoculated. The experiment lasted 542 days and no change in the bovine bacillus was found at the end of the experiment. A similar result was obtained by passage in baboons.

Appendix, Vol. IV, p. 390.

In further experiments with the human tubercle bacillus nine separate viruses were used. With six of the viruses passage experiments were carried out on calves, the number of animals included in each experiment varying from two to seven and the total duration of the residence of the bacilli in the calf's body varying from 247 to 512 days. There was no alteration in the characters of the bacillus at the end of the passage in any of the cases. After continued residence in one case for 484 days in the bodies of three rabbits consecutively, and in another after 725 days single residence in the body of one rabbit the human cultures were found unchanged. Similar results were obtained in two experiments on the rat after residence in the one case for 454 days in the body of one rat, and in the other for 1614 days in the bodies of eight rats consecutively. Single residences in a cow for 529 days, in a pig 378 days, a guinea-pig 320 days, a dog 413 days, produced no change in the characters or virulence of the cultures of the human bacillus.

Appendix, Vol. I, p. 55.

These particular experiments, therefore, failed to effect any modification in the bovine or human tubercle bacillus.

71. As regards experiments directed to modify the virulence of the avian tubercle bacillus similar negative results were obtained. Single residence in the horse, calf, goat, pig, monkey, cat, dog, rat, mouse, rabbit, and guinea-pig showed no change in the cultural characters nor in the virulence of the avian bacillus originally inoculated. Passage experiments were performed on calves with the culture of Virus A. X, which was obtained from the lung of a rabbit inoculated from natural tuberculosis in a fowl. From one of the calves of this series a culture obtained from the bronchial gland was bovine in character, while in the same animal a typical avian culture was obtained near the seat of inoculation. There can be little doubt that this was not a case of modification, but one of accidental infection of the calf by the bovine bacillus. Other experiments were performed with avian bacilli obtained from pig tuberculosis, and in some of these experiments the bovine tubercle bacillus, and in one case the human tubercle bacillus, was obtained from some of the lesions of the animals into which the culture derived from the pig lesion had been introduced. These results, which are set forth in the Appendix, were obtained in only a few experiments and were so discordant that we cannot draw any conclusions from them.

Appendix, Vol. IV, p. 385.

72. In cases of internal human tuberculosis we found a certain number which showed a mixture of human and bovine tubercle bacilli, and in the pig there was one case in which there was a mixture of bovine and avian tubercle bacilli. When separated, the bacilli from these cases were found to correspond in their characters to the bovine, human and avian types. Although it might be urged that the mere finding of the two types in a lesion indicated the occurrence of a process of modification in one or other type, yet we found no transitional types in the lesions

Appendix, Vol. III, pp. 12 18, and 151.

of internal tuberculosis in the human being, nor in the pig any but doubtful suggestion of such transition. The only variation from the three types which we have found in our extended investigations have occurred in cases of lupus and in equine tuberculosis.

SECTION X.

Consideration of the Results in relation to the Terms of Reference.

73. The questions that were referred to us for investigation and report are as follows :—

1. " Whether the disease in animals and man is one and the same ;
2. Whether animals and man can be reciprocally infected with it ;
3. Under what conditions, if at all, the transmission of the disease from animals to man takes place, and what are the circumstances favourable or unfavourable to such transmission."

We have attempted to answer these questions by investigating cases of natural tuberculosis in man, and by studying the disease in animals as it occurs naturally in them as well as when produced by experimental means. Our investigation has dealt not only with the naked-eye and microscopical appearances of the diseased tissues, but also with the tubercle bacillus itself—the essential cause of the disease. Separating the bacillus from the lesion, we have obtained it in pure culture and studied the variations of its growth under artificial conditions and the results produced by it when injected into animals of various species. Tuberculosis being a disease affecting not only man but also domestic animals such as cattle, horses, pigs and poultry, and certain other animals when kept in captivity, our investigation has covered a wide range of tuberculous disease, and enabled us to make a careful comparison of the conditions of tuberculosis as it occurs naturally in man and in animals. In three Interim Reports presented during the progress of our investigation we set out certain results as they were arrived at, expressing opinion on the facts before us ; and we have already, in the preceding Sections of this our Final Report, summarized those earlier results together with others not previously recorded. It is now necessary to consider how far the total results of our investigation afford material for definite reply to the questions put to us.

First Term of the Reference.

74. The first question is :—Whether tuberculosis in animals and man is one and the same.

The morbid conditions in man and animals which are embraced under the term tuberculosis are all bacterial in their origin, and the question of the identity or non-identity of a case of tuberculosis in one animal with a case in another animal of the same or of a different species depends upon the identity or non-identity of the bacilli responsible for the lesions in each case. It therefore becomes necessary to inquire whether it is possible to arrange bacteria in sharply defined groups corresponding with what are called species in the case of the higher plants and animals, or to affirm of any two bacteria that they are identical in the sense that all members of the canine species are identical. The characters which are generally relied upon to fix the species of bacteria are their morphology (including size and form), their appearances in artificial culture, and their pathogenic properties or capacity for causing disease in various species of animals. As in the classification of the higher plants and animals, so also in the classification of bacteria, morphological characters have the greatest value, and no two organisms which constantly differed in form and size could be considered identical or belonging to the same species, even though they were indistinguishable in every other respect. In spite of their minuteness and the simplicity of their structure some bacteria present well-marked morphological differences as compared with others, and in such a case non-identity is obvious, and classification presents no difficulty. Classification is still easy in spite of morphological identity when bacteria differ markedly in cultural and pathogenic characters, but it becomes difficult when bacteria that are morphologically indistinguishable exhibit only minor differences in respect of their cultural and pathogenic characters.

The particular case which we are now considering is exactly of that nature.

Leaving aside for the moment the question of the relationships of the bacilli of avian tuberculosis, it has to be admitted that the human and bovine types of bacilli are morphologically indistinguishable, but appreciably different in respect of their cultural characters and their capacity for causing disease in various species of animals. The question of the identity or non-identity of these two types therefore clearly depends upon the importance which it is permissible to attach to their cultural and pathogenic differences, and this in turn on the fixity or variability of the differences in question. If these differences are not constant they cease to be of value for classification, but if according to all the available evidence they are constant, the human and bovine types of tubercle bacilli must be considered distinct, and the diseases which they cause as not identical, that is to say not one and the same.

At an earlier part of this Report we have discussed the question whether the human and the bovine types are stable in respect of their cultural characters and pathogenic properties. With regard to the first of these we need only repeat here that the only difference in respect of cultural characters between the two types is that the human type exhibits a greater luxuriance of growth on all the different media which we have employed in making comparisons, and that although this difference is not maintained with absolute constancy, we have not in our cultural experiments observed any case in which the mode of growth of the one type became so far modified as to be indistinguishable from the mode of growth usually exhibited by the other. But the point must be emphasised that the bacilli which we have referred to the bovine type vary considerably among themselves in respect of luxuriance of growth, and that the gap which separates those of them that grow most abundantly from bacilli of the human type is not a wide one.

The bovine tubercle bacillus produces a fatal tuberculosis in cattle, rabbits, guinea-pigs, chimpanzees, monkeys, goats and pigs.

The human tubercle bacillus readily produces a fatal tuberculosis in guinea-pigs, chimpanzees and monkeys, but causes, even when administered in large doses, only slight and non-progressive lesions in cattle, goats and pigs. Its effect on rabbits is not uniform, for whilst in the majority of cases these animals are only slightly affected, in others extensive and fatal tuberculosis results in them from the inoculation of the human tubercle bacillus.

In other words, we have always found that guinea-pigs, chimpanzees and monkeys are all highly susceptible to the effects of either the human or the bovine tubercle bacillus and that the disease produced in these animals by both types is histologically and anatomically identical.

Obviously it has not been permissible to induce tuberculous disease experimentally in the human subject by the injection of bovine tubercle bacilli, and no opportunity presented itself to us of examining any case of accidental infection in which the bovine tubercle bacillus entered the human body through the skin and set up a generalised disease. But we have investigated many instances of fatal tuberculosis in the human subject in which the disease was undoubtedly caused by a bacillus of the bovine type and by nothing else. We have compared the lesions from such cases with those obtained from parallel cases of fatal tuberculosis in which the human tubercle bacillus alone was discovered. Except for the difference in the type of bacillus found in them, these two groups of cases presented similar features ; the clinical histories of the patients were alike, the cases all terminated fatally, and the lesions examined after death were found to be anatomically indistinguishable. Man must therefore be added to the list of animals notably susceptible to bovine tubercle bacilli.

Chief among the differences between bovine and human tubercle bacilli is, of course, difference of virulence towards certain animals. Why, it may be asked, is the human bacillus, though as virulent for the monkey and the guinea-pig as is the bovine, far less virulent than that bacillus for the calf, goat, and pig. Is the human bacillus a bovine bacillus which, through some cause or combination of causes, has become modified, and, if so, is its degradation in this sense permanent ?

We have recorded (paragraphs 69 and 70) our repeated attempts to transmute the bovine bacillus into the human bacillus and *vice versâ*. Most of these attempts failed altogether, a few only were equivocal ; we found indeed that under the conditions contrived by us both types of bacilli remained remarkably stable, alike as regards their growth on artificial media and their virulence for animals. Thus, we are inclined to regard transmutation of bacillary type as exceedingly difficult if not impracticable of accomplishment by laboratory procedure, though in view of certain instances in which we obtained from one and the same human body both types of bacillus, we are not prepared to deny that the transmutation of one type into another may occur in nature.

With respect to the question of the stability of the pathogenic properties which distinguish the two types, we must again refer to the exceptional characters possessed by certain of the bacilli which were isolated from cases of lupus and equine tuberculosis. In some of these cases the bacilli had the ordinary cultural characters of the bovine type, associated with a degree of virulence for the calf and rabbit no greater than is usually exhibited by the human type. We have already given reasons for declining to accept these exceptional bacilli as distinct fixed types, and if that view of them is excluded they must be regarded as either modified human or modified bovine bacilli. On the former assumption they had acquired the character of growth ordinarily exhibited by the bovine type, and on the latter assumption they had lost the higher degree of virulence for certain animals which is characteristic of the bovine type. The latter appears to be the more probable explanation, and if that view be accepted the discovery of these exceptional bacilli makes it impossible to regard difference of virulence for the calf and rabbit as sufficient to establish the non-identity of the human and the bovine types.

There would therefore remain only slight cultural differences on which to found the conclusion that the human and the bovine types represent two distinct organisms. We prefer to regard these two types as varieties of the same bacillus, and the lesions which they produce, whether in man or in other mammals, as manifestations of the same disease.

But while we regard the point which we have just considered as one concerning which there is room for difference of opinion, there is an aspect in which tuberculosis in men and in cattle must unquestionably be pronounced one and the same disease. Whether one prefers to regard bovine tuberculosis and the cases of tuberculosis in man which are caused by the human type of bacilli as varieties of the same disease or as independent diseases, there can be no question that human tuberculosis is in part identical with bovine tuberculosis. Our researches have proved that in a considerable proportion of cases of the human disease the lesions contain, and are caused by, bacilli which are in every respect indistinguishable from the bacilli which are the cause of tuberculosis in cattle. In all such cases the disease therefore is the same disease as bovine tuberculosis.

There remains the question whether avian tuberculosis and bovine tuberculosis, or avian tuberculosis and the tuberculosis caused by the human type of bacillus, are one and the same disease. In this matter there does not appear to us to be in the present sufficient ground for answering the question in the affirmative.

SECOND TERM OF THE REFERENCE.

75. In the second term of our Reference we were asked :—Whether animals and man can be reciprocally infected with tuberculosis ; that is, whether the disease known as tuberculosis can be communicated direct from man to animals and from animals to man. The question thus presented to us was one of exceptional difficulty. For though the liability of animals to infection from man could be tested in detail by direct experiment, man's liability to infection from animals remained of necessity matter only of inference. Certain instances have, it is true, been reported in which suspicion had arisen that man had become infected through contact with tuberculous cattle, but the evidence afforded by these cases, notwithstanding that they had been carefully investigated, could not be accepted as unequivocally positive in character. Accordingly the transmissibility of tuberculosis of the three several types has had to be judged of by the behaviour of the bacilli representing them when introduced, each in separate series, into the bodies of a variety of animals.

By subcutaneous inoculation the human type has been found transmissible in some degree to many different species of animals, but for most of them transmission has been effected only by the employment of large doses. And moreover in some species of animals the lesions thus induced were either local or sparsely distributed and non-progressive in character. The animals that we have found to be especially refractory to the human tubercle bacillus administered by subcutaneous inoculation are cattle, pigs, and fowls, and these animals are often even more refractory, or are indeed practically immune, when the bacilli are administered, even in large amounts, with their food. Corroboration of this high degree of resistance to human tubercle bacilli on the part of cattle, pigs and fowls is afforded by the circumstance that so far as our investigation of tuberculosis naturally occurring in the lower animals has gone we have not in a single instance detected the human type of tubercle bacillus in cattle or in fowls, and but rarely in pigs. Rabbits are not so resistant to the human tubercle bacillus, which is capable of producing in them progressive and fatal tuberculosis (page 6).

In strong contrast to this small liability of certain of the lower animals to tuberculosis of the human type is the susceptibility of animals generally to infection by the bacillus of the bovine type (whatever the source, lower animal or man, of such bacillus). Over a very wide field of experiment in this connection, the only animals that we have found at all uniformly resistant to this type of bacillus are the common fowl, the rat and (to a less extent or at least less uniformly) the dog. And similarly our investigations of tuberculosis naturally occurring in lower animals indicate the great preponderance of the bovine type among them.

In cattle suffering from tuberculous disease acquired other than by experimental means, we have in no single instance detected any but the bovine bacillus.* This is also the type of bacillus found in progressive tuberculosis in the pig, though this animal is capable of harbouring (while perhaps not encouraging) the human and avian types of tubercle bacillus. So far as our experiments show, the chimpanzee, an animal closely related to man, is equally susceptible to the bovine and human tubercle bacillus, the effects produced by them in this animal both by feeding and inoculation with parallel doses being closely alike.

As regards the avian type of tubercle bacillus, reciprocity among animals to this infection hardly calls for notice. Though the fowl and other birds are highly susceptible to tuberculosis of this type, mammals generally, with the exception of the rabbit and mouse, and, perhaps to a less extent, the pig and goat, would appear almost absolutely resistant to it. The monkey and the guinea-pig, both of them highly susceptible to bovine and human tubercle bacilli, are notable instances of this.

Taking these facts into consideration together with those others already discussed in relation to the first term of our Reference, and for the above reason excluding the fowl and other birds from further consideration in this connection, we must conclude that mammals and man can be reciprocally infected with the disease (tuberculosis). The possible danger to man through reciprocity in this sense was, of course, the more important question presented to us, and as we have conclusively shown that many cases of fatal tuberculosis in the human subject have been produced by the bacillus known to cause the disease in cattle, the possibility of such infection cannot be denied.

And the importance of this conclusion is not diminished by the fact that the majority of such cases examined by us occurred in young children, or by the merely local results following the administration of the human type of bacillus to bovine animals. Bovine animals are not completely immune to the human tubercle bacillus, and adult human beings can be infected with the bovine type, even the pulmonary form of the disease in man being sometimes caused by the bovine tubercle bacillus.

THIRD TERM OF THE REFERENCE.

76. The third question with which we are called upon to deal is :—

Under what conditions, if at all, the transmission of tuberculosis from animals to man takes place, and what are the circumstances favourable or unfavourable to such transmission.

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* *See* footnote on page 4.

Transmission of tuberculosis from animals to man must obviously be mainly dependent on the susceptibility of any given animal to this disease and on the opportunities afforded such animal for transferring its acquired and developed infection to the human subject. From what we have already said, man must clearly be regarded as being liable to risk of infection from at least two of the three types of tubercle bacilli, the human and the bovine. In this connection it will be convenient to discuss each type separately.

Avian Tuberculosis.—Prima facie, man might be regarded as at some risk from this form of tuberculosis owing to his food relations with fowls and certain other birds, and the fact that we have in more than one instance discovered the avian tubercle bacillus in the bodies of pigs might also be considered a matter of importance. But in no single instance have we found the avian tubercle bacillus in the lesions of tuberculosis in the human being, whilst man's comparatively near relative, the monkey, would appear from our experiments to be highly resistant to tubercle bacilli of this type. The pig is the only mammal in which we have found the avian bacillus in the lesions of naturally acquired tuberculosis, but possible danger to man from this source would appear to depend on an ability not yet demonstrated of this animal to bring about modification or alteration of this type of tubercle bacillus in the direction of greatly enhancing its virulence for man. We must conclude, as the result of our investigations, that the unmodified avian tubercle bacillus is a negligible factor in the production of human tuberculosis.

Human Tuberculosis.—In so far as tuberculosis of this type in animals lower than man has resulted from infection contributed to them by man himself, man has been multiplying in bodies other than his own that type of tubercle bacillus to which he is seemingly most prone, and thus increasing his chances of death by tuberculosis. But, as has been shown, animals, domestic and other, which have been found capable of suffering from severe generalised tuberculosis of the human type are comparatively few; and further, none of these active multipliers of human tubercle are common food animals. The bovine animal for instance is not an active multiplier of the human tubercle bacillus, being highly refractory to this infection; and the cow herself, however prone she may be when the subject of bovine tuberculosis to excrete bovine bacilli in her milk, has never under natural conditions been convicted of eliminating in this way the human tubercle bacillus. Experimentally, it is true, the human bacillus has been made to appear in the milk of the cow and goat, but for securing this end very large doses of culture have been requisite. Probably only when the cow or goat has received a large dose of tuberculous material derived from man does the human tubercle bacillus escape into the blood stream of the animal, reach her milk sinuses, and become eliminated with her milk.

Nevertheless, it is not to be affirmed with confidence that man is wholly free from risk through animal food of infection with that type of tubercle bacillus to which he appears most prone, though the degree of danger to him in this sense must remain for the present undetermined. The pig, though not capable in our experimental experience of fostering tubercle bacilli of the human type except in a minor degree, may have to be regarded as a possible source of the disease caused in man by that type of bacillus; for the reason that particular glands of the pig's body, which are likely to enter into certain prepared foods, do on occasion yield tubercle bacilli of the human type.

Bovine Tuberculosis.—Before dealing with the conditions affecting the direct transmission of tuberculosis from bovine animals to man, one other potential source of infection of man with the bovine type of the tubercle bacillus must be referred to. The pig is, besides the bovine, the only animal commonly used for food by man in which during our investigation we have found the bovine tubercle bacillus producing the progressive lesions of the natural disease. We found this bacillus in a number of cases of swine tuberculosis sufficient to justify us in calling attention to the danger without entering into a discussion as to its extent. Bovine tubercle bacilli are infective to human beings, and we have no reason to suppose that they can be rendered less so by previous residence in the bodies of pigs.

During the course of our inquiry we investigated material obtained either post-mortem or by operation from 146 individual cases of persons suffering from tuberculosis; a total which does not include the two viruses consisting of sputum collected daily from a varying number of patients. But some of those 146 have been excluded from our final conclusions for reasons already set out on page 9, and certain others of them, though dealt with in detail in our Appendix, are not considered in this Report, the investigations in which material from them was employed having but an indirect bearing on the terms of our Reference. Thus the actual number of cases, representing the various clinical manifestations of tuberculosis commonly found in man, that have passed under strict observation and on which our conclusions are based, is 128.

So far as these 128 cases have been examples of tuberculosis in the adult, and especially when they have been cases of pulmonary tuberculosis, the lesions of the disease when fatal have been referable with few exceptions to human bacilli. Only rarely has a pulmonary lesion in adult man yielded the bovine bacillus. Our experience of abdominal tuberculosis in the human subject has been very different, especially as regards children. Of young children dying from primary abdominal tuberculosis, the fatal lesions could in nearly one half of the cases be referred to the bovine bacillus, and to that type alone. In children, too, and often also in adolescents, suffering from cervical gland tuberculosis, a large proportion of the cases examined by us could be referred to the bovine tubercle bacillus. We have already in an earlier portion of this Report referred to the importance of infection by the bovine type of tubercle bacillus in cases of lupus occurring in adolescents and children.

Whatever, therefore, may be the animal source of tuberculosis in adolescents and in adult man, there can be no doubt that a considerable proportion of the tuberculosis affecting children is of bovine origin, more particularly that which affects primarily the abdominal organs and the cervical glands. And further, there can be no doubt that primary abdominal tuberculosis as well as tuberculosis of the cervical glands is commonly due to ingestion of tuberculous infective material.

Judging by our feeding experiments there would appear to be strong presumption that as regards most animals comparatively large doses given either singly or by frequent repetition are necessary to produce by ingestion acute progressive generalised tuberculosis, though we have recorded instances in which a very small dose administered but once has produced this result. Applying a like presumption to man (and our observations on the monkey and chimpanzee in this connection afford warrant for so doing) it may be asked in what way are children, the members of the human family who are especially liable to exhibit acute fatal tuberculosis commencing as an abdominal affection, most likely to obtain a large and fatally infective dose of tubercle bacilli ?

As already indicated by us, to this question there can be but one answer :—namely that the evidence which we have accumulated goes to demonstrate that a considerable amount of the tuberculosis of childhood is to be ascribed to infection with bacilli of the bovine type transmitted to children in meals consisting largely of the milk of the cow.

In many cases of abdominal tuberculosis and in tuberculosis of the cervical glands, however, it must be recollected that the child may be injured by the ingestion of bovine tubercle bacilli in milk without a fatal result occurring. The cases of abdominal tuberculosis examined by us had all been fatal, that is death occurred from a generalised tuberculosis or from some local condition resulting, with possibly two exceptions, from tuberculosis of the abdomen. But many cases of abdominal tuberculosis in children recover, though what proportion of these is due to the bovine bacillus and what to the human, we have no means of knowing at present. The cases of cervical gland tuberculosis investigated by us were all cases that recovered or were recovering after operation, and a large proportion of them were bovine in origin.

Although the potency of tuberculous cow's milk in the causation of the tuberculosis of infancy and childhood is clearly demonstrated, in our examination of material from 55 cases of tuberculosis in adolescents and adults we have found rarely in the former and extremely seldom in the latter the bovine bacillus colonising the fatal lesions.*

Instead we found abundantly in these lesions none but the human bacillus, a circumstance, which, if considered alone, might tend to discount the extent of the danger to the adult human subject not only of the milk of tuberculous cows but also of the flesh of that and other animals capable of fostering the bovine tubercle bacillus. But it must be remembered that we have found cases of tuberculosis in adult man, sufficiently extensive to incapacitate the patient for the ordinary duties of life and in two instances ending fatally, in which we were able to attribute the disease solely to the effects of the bovine tubercle bacillus. Though of the 55 cases of adolescent and adult tuberculosis which came under scrutiny no more than 5 yielded bacilli of the bovine type, we cannot say that this figure adequately represents the proportion of like cases obtaining among the tuberculous population generally.*

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* *See* footnote next page.

77. Meanwhile we, in view of the evidence adduced by us, regard ourselves as called upon to pronounce on administrative measures required in the present for obtaining security against transmission of bovine tubercle bacilli by means of food. In the interests therefore of infants and children, the members of the population whom we have proved to be especially endangered, and for the reasonable safeguarding of the public health generally, we would urge that existing regulations and supervision of milk production and meat preparation be not relaxed; that on the contrary Government should cause to be enforced throughout the kingdom food regulations planned to afford better security against the infection of human beings through the medium of articles of diet derived from tuberculous animals.

More particularly we would urge action in this sense in order to avert or minimise the present danger arising from the consumption of infected milk. And in this connection it may be convenient for us to repeat certain facts observed by us in reference to the conditions tending to the elimination by the cow of bovine tubercle bacilli in her milk; facts in our opinion of such importance that they formed the subject of our Third Interim Report.

Bovine tubercle bacilli are apt to be abundantly present in milk as sold to the public when there is tuberculous disease of the udder of the cow from which it was obtained. This fact is, we believe, generally recognised though not adequately guarded against. But these bacilli may also be present in the milk of tuberculous cows presenting no evidence whatever of disease of the udder, even when examined post-mortem. Further, the milk of tuberculous cows not containing bacilli as it leaves the udder may, and frequently does, become infective by being contaminated with the fæces or uterine discharges of such diseased animal. We are convinced that measures for securing the prevention of ingestion of living bovine tubercle bacilli with milk would greatly reduce the number of cases of abdominal and cervical gland tuberculosis in children, and that such measures should include the exclusion from the food supply of the milk of the recognisably tuberculous cow, irrespective of the site of the disease, whether in the udder or in the internal organs.

We desire to express our sense of the great value of the services rendered to the Commission by our officers, professional and other.

To our Secretary, Dr. E. J. Steegmann, we are indebted not only for further unwearied diligence in our behalf during additional years, but also for exercise by him throughout the whole period of this Commission of administrative capacity of the highest order.

The work of our several investigators is summarised by each (above his signature) in those volumes of the Appendix to this Report in which details of his particular research are recorded. The volumes in question are sufficient testimony to the painstaking accuracy and intelligent resourcefulness of these experts. In this place, however, we would express our special appreciation of Dr. A. Stanley Griffith's original and highly important researches on Lupus and his admirably effective scrutiny of anomalous viruses; Dr. Frederick Griffith's investigation of Equine tuberculosis; Dr. Arthur Eastwood's histological researches; and also of the importance of the work carried out jointly by Dr. A. Stanley Griffith and Dr. Frederick Griffith in connection with the tuberculosis of swine.

The duties undertaken by Dr. Hammond-Smith are referred to in detail in the Memorandum accompanying this Report. We wish here to record our sense of the great value of his services.

Our non-professional administrative officers and our laboratory assistants have each and all of them rendered throughout admirable and faithful service. Among the former we are on these grounds particularly indebted to Mr. C. F. Fox and Mr. J. Keddie ; among the latter to Mr. C. Attoe.

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* The 55 cases referred to include only those of tuberculosis other than lupus. Cases of lupus coming under observation in adolescent and adult patients numbered 10, 3 of which yielded tubercle bacilli presenting the cultural characters of the bovine type though possessing less virulence for the calf and rabbit than the bovine tubercle bacillus.

Finally we again record our grateful recognition of the keen interest in and never failing generosity towards our researches which have ever been conspicuously manifested by Lord Blyth. By his ungrudging hospitality, during a decade of years, in placing at our disposal his Stansted Farms he has enabled our investigations to be carried on untrammelled by outside interference or objection, and (a matter of great practical importance) absolutely without risk of transferring infection to animals the property of neighbours.

(Signed) W. H. POWER, *Chairman.*
G. SIMS WOODHEAD.
SIDNEY MARTIN.
J. McFADYEAN.
RUBERT BOYCE.

EDWARD J. STEEGMANN, *Secretary.*
June, 1911.

MEMORANDUM.

In the Introduction to the Second Interim Report the procedure adopted by the Commissioners for carrying out their investigation was explained, and the Farms and Laboratories at Stansted were described. An account was also given of the methods of experiment, of the precautions taken to obtain healthy animals for experimental purposes and of the means used for procuring the material required for research. Though not necessary to repeat all that was there said, no alteration having been made in any important particular in the period that has elapsed since that Report was issued, it may be convenient to re-state briefly certain essential facts connected with the practical administration of the inquiry.

During the whole of the time occupied by the Commission in investigating the questions contained in the several terms of their Reference, all the experimental work on which conclusions have been based was carried out in the Stansted Laboratories and Farms by resident investigators working under the direct supervision and control of the Members of the Commission. A few independent investigations were, it is true, entrusted to other observers, but these affected matters in the nature of side-issues, and no additional positive facts bearing on the main points of the investigation having been thus established the results obtained were not taken into account by the Commission.

At Stansted, three widely separate places were used by the Commission for research work; each was in charge of an investigator, with an adequate staff of assistants under him, and no communication was permitted between those where experimental animals were kept except under strict rule and supervision.

The whole of the land occupied by the Commission at Stansted, the house known as Royalcot, used for administrative purposes as well as for the accommodation of Members of the Commission when visiting Stansted, and the farm buildings, were lent by Lord Blyth, without any expense to the Government for rent, rates, or taxes. In addition, he allowed the Commissioners to erect laboratories and animal houses, and to alter in any way they pleased the existing buildings. But at Blythwood the buildings that had been previously erected by Lord Blyth for his own stock proved so eminently suitable for the purposes of the investigation that very little modification was required; indeed it would have been difficult to find, even apart from the question of cost, any places so well adapted for the practical experimental work as those provided by the far-sighted generosity of Lord Blyth.

Animal experiments were only carried out at two of these places, Walpole and Blythwood Farms.

Walpole Farm was at first used solely for the investigation of the tuberculosis of bovine animals, and no other work carried out at this farm was considered in the Second Interim Report of the Commission. But before the issue of that Report the practical inquiry in connection with Swine Tuberculosis had been commenced at Walpole, and the preliminary experiments relating to the subject of Immunity had been completed there.

In the present and final Report, four separate investigations that were carried out at Walpole are dealt with, namely, those on Swine, on Equine, and on Avian Tuberculosis, and an investigation of a limited number of viruses obtained from natural tuberculosis in various animals. In addition, some of the practical work on which the views of the Commission on modification are based was performed at Walpole. No viruses of known human origin were at any time received there.

In course, however, of the researches into Swine Tuberculosis, three pigs, material from which had been sent to Walpole Farm for examination, were found to have been the subjects of tuberculosis of the human type; and in the course of the immunity investigations a number of experimental calves, which had previously been vaccinated with human viruses at Blythwood, were transferred to Walpole for the subsequent test inoculation with bovine tubercle bacilli. But, with one exception, none of these animals was taken to Walpole before 1906, and in the case of each of them stringent precautions were adopted to prevent possible contamination of other viruses. These immunity calves were kept apart from all other animals. After the termination of the investigations particularly connected with Bovine Tuberculosis, four viruses, received from the Zoological Gardens and other sources, were found to contain tubercle bacilli of human type (Appendix, Vol. IV., p. 149). The experimental work at Walpole farm, which had commenced in May, 1902, was brought to an end in March, 1909.

At Blythwood there was carried out during eight years the whole of the experimental work in connection with human tuberculosis. Practical work commenced there in April, 1902, and was brought to an end in September, 1910, though by the kindness of Lord Blyth the Commission remained in occupation of the laboratory at Blythwood for some months longer.

The third place occupied by the Commission at Stansted was known as Royalcot, and, so far as the scientific work was concerned, consisted of laboratories only, without any accommodation for experimental animals. The Royalcot laboratories were used only for the histological examinations of tissues and for the comparative investigation of cultures sown in the first instance at Blythwood or at Walpole, or which were grown at Royalcot from material supplied from one or other of these places. The work at Royalcot commenced early in January, 1903, and lasted till nearly the end of the year 1909, a total period of about seven years.

Walpole and Blythwood farms being licensed for the performance of experiments on living animals were repeatedly visited by the Inspector appointed by the Home Office. All the investigators, with the exception of Dr. Eastwood, were fully licensed to perform animal experiments, and Dr. Steegmann also held a licence for each place, as such necessary inoculations that had to be done during any temporary absence of one or other of the resident investigators were performed by him.

At the time of the issue of the Second Interim Report, as stated therein in the Introduction, Blythwood Farm was in charge of Dr. A. Stanley Griffith,* and Walpole Farm of Dr. F. Griffith, Dr. Eastwood being at that date responsible for the work carried out at Royalcot. The Commission have been so fortunate as to retain until practically the end of their labours the services of all these resident investigators. Dr. Eastwood, having finished the inquiries entrusted to him, resigned his appointment with the Commission at the end of December, 1909. Dr. F. Griffith, after the termination of the practical work he had carried out at Walpole, was engaged for a further period of three months finishing his written reports. Dr. A. Stanley Griffith, although not occupied at Blythwood after the end of July, 1910, gave up much of his time to the service of the Commission during many months subsequently, and his assistance in the deliberations of the Commission and in the preparation of the Report proved of very great value.

For a long time, in fact during the whole of the period during which material for experimental investigation was being received at Stansted, Dr. Hammond-Smith acted as clinical observer and collector. Hardly ever was any material obtained from a post-mortem examination or an operation at which he had not been present, and the fact that nearly all the specimens were received at the laboratories in a condition rendering them suitable for experimental use and free from accidental contamination was in large measure due to his skill and careful precaution. The operation patients, frequently kept under observation for months and in some cases for over two years, were visited by him, and, whenever possible, the family histories of the patients were verified by personal interviews with relations or with parents of children. Dr. Hammond-Smith's tact and patience overcame many difficulties that otherwise might have proved of great disadvantage.

Mr. C. F. Fox, appointed at an early stage of the work at Stansted to carry out the clerical work at Blythwood Farm, acquired a knowledge of scientific methods that rendered his assistance in many other ways of great advantage. After the cessation of the practical investigation at Stansted he was transferred to London, and co-operated with the Secretary in the preparation for the press of the various volumes of the Appendix.

Mr. Keddie, throughout the whole of the time that the Commission was in occupation at Stansted, was in charge of the non-scientific administrative work. His wide knowledge and experience in the management of cattle was of the utmost value in obtaining and keeping healthy the stock required for experimental purposes.

No alteration had to be made in the several staffs of skilled assistants employed in the laboratories, and the fact that all the laboratory workers were experienced and trained in the special methods of the Commission has been an important element in ensuring uniform accuracy of the investigations. Mr. Attoe, the head assistant at Blythwood, engaged by the Commission from the beginning, remained till the whole of the work there was finished ; and after Dr. A. Stanley Griffith left Stansted until it was finally decided that no further investigations were to be undertaken, he was in sole charge of the laboratory and such viruses as it was still desired to keep alive in culture.

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* Previously Dr. Cobbett had carried out the work at Blythwood.

The methods adopted for collecting material to be used for investigating bovine and human tuberculosis have already been described (Second Interim Report, page 47). As regards tuberculosis naturally occurring in other animals the sources of material subjected to experiment were as follows :—

SWINE TUBERCULOSIS.

All the specimens of natural tuberculosis in pigs that were utilised for this investigation were obtained by Dr. Hammond-Smith, who personally examined every carcass from which lesions were taken. Of the 63 cases detailed in the table of Origins (Appendix Vol. III, page 153), 58 came from the Metropolitan Meat Market in London and 5 from the Corporation Slaughter House in Birmingham. The first specimen was received at Stansted on March 5th, 1905, and the last on July 19th, 1907.

At both these places special facilities were afforded the Commission for collecting the material required. At the Metropolitan Meat Market a room was set aside in which bottles and boxes could be stored and where the specimens could be isolated and packed. Dr. Hammond-Smith visited the Market from time to time at uncertain intervals, and accompanied the Chief Veterinary Inspector on his examination of the carcasses already slaughtered and partially dressed. The pigs came to the Market alive and a preliminary official veterinary inspection of the living animal prevented any pig that did not appear to be in good health and condition being admitted to the slaughter-house. On no occasion was tuberculous disease suspected in any pig before it was killed. As a rule not every carcass was systematically examined by the Veterinary Inspector, but mainly those in which the butchers, men of great experience, had reason to suspect some abnormal condition. In the majority of instances the viscera had been removed from the carcasses and put aside in groups for the veterinary inspection ; thus, in the event of disease being detected in any of the organs, it was not always possible for Dr. Hammond-Smith to identify with certainty the particular carcass from which such tuberculous organ had been taken. It is, therefore, important to note that in many of the cases where the single tuberculous organ found, such as a submaxillary or bronchial gland, was used as the material for investigation, it cannot be stated confidently that no tuberculous disease was present elsewhere in the same animal, even though none had been detected in the routine market examination ; it was obviously impossible to carry out in the slaughter-house a detailed and careful post-mortem examination of every pig killed there such as was always made at Stansted.

Comparatively few cases of generalised tuberculosis in swine being met with at the Metropolitan Meat Market, arrangements were made by Dr. Hammond-Smith by which he could be informed of any that occurred at the Corporation Slaughter House in Birmingham. By this means five cases of generalised tuberculosis were obtained, information concerning them being sent by telegram. On receipt of the notice Dr. Hammond-Smith went to Birmingham and despatched the specimens direct to Stansted. In all the five cases the animal had been slaughtered before his arrival, but the carcasses, together with all their viscera had been set aside in each instance for his examination.

The thanks of the Commission are due to the Authorities of both these slaughter-houses for their assistance.

One other point in connection with the investigation of swine tuberculosis deserves particular notice. Many hundred carcasses of pigs were examined by Dr. Hammond-Smith, but the number of instances in which tuberculous disease was found is in no way representative of the amount of disease existing amongst pigs generally. For all the animals had been sent to the slaughter-house for the express purpose of being forthwith killed and sold for food, and it is extremely unlikely in view of the strict inspection to be anticipated there that any animal would be so sent which the owner did not honestly believe to be quite sound and healthy.

No pigs that during life had shown signs of disease were at any time used by the Commission to provide material for the investigation of natural swine tuberculosis.

EQUINE TUBERCULOSIS.

The material of Equine Tuberculosis used for the investigation was obtained from five cases of the disease occurring naturally in the horse. In two of the cases the animals had general tuberculosis, in two the mesenteric glands only were affected, and in one case the spleen alone showed evidence of the disease.

All the specimens were obtained from the Royal Veterinary College; in some cases the tuberculous horse had been examined post-mortem there. A description of the material received at Walpole Farm will be found in the table of origins of the Equine Viruses on page 10 of Volume IV. of the Appendix.

AVIAN TUBERCULOSIS.

The material from which the avian viruses were obtained came in the majority of instances from the bodies of birds that had either died of tuberculosis or had been killed and proved on post-mortem examination to be tuberculous. The birds were of various species and the details are given in the table of Origins (Appendix, Vol. IV., page 174). In addition avian tubercle bacilli were isolated from six pigs tuberculous lesions of which had been sent to Walpole. In these animals the particular type of bacillus responsible for the tuberculous lesion or lesions had not, of course, been suspected. No naked-eye difference can be detected between merely local lesions produced in the pig by the avian tubercle bacillus and similar lesions produced by bovine or by human tubercle bacilli. The details of the six porcine viruses that yielded avian tubercle bacilli will be found in the report on Swine Tuberculosis (Appendix, Vol. III., page 145).

CASUAL TUBERCULOSIS OF CERTAIN MAMMALS.

The origins of the material used in the investigation of viruses obtained from casual tuberculosis of certain mammals are stated at the beginning of the particular report relating to that investigation (Appendix, Vol. IV., page 151). It should be noted that no special search was made for tuberculous disease in these animals, but the opportunity occurring, the viruses were used for investigation.

HUMAN TUBERCULOSIS INCLUDING LUPUS.

The actual lesions used for the continued investigation of cases of human tuberculosis other than Lupus were obtained from post-mortem examinations or after operations in the same manner and with the same precautions as were adopted previously (*see* Second Interim Report, page 47), but in the matter of the 28 viruses that consisted of sputum from individual human cases special precautions were taken. These have already been referred to in the present Report (page 12), but it may be noted in addition that the patients themselves took great interest in the investigation and willingly co-operated in carrying out the restrictions as to diet imposed upon them. Dr. A. S. McNalty, the Resident Medical Officer at Brompton Hospital, rendered assistance of great value in this particular investigation, and thanks of the Commission are due to him and to the Nursing Staff of the Hospital. Without such help it would not have been possible to ensure observance of the strict precautions that were prescribed to prevent possible contamination of the sputum. The only points taken into account in selecting the patients for sputum investigation were that so far as could be ascertained by clinical examination the disease in each one should be limited to the thorax, and that previous microscopic examination of the sputum should have revealed the presence therein of acid-fast bacilli in considerable numbers.

Material for the investigation into Lupus was obtained by Dr. Hammond-Smith. Considerable difficulty was experienced in discovering a sufficient number of patients suffering from this form of tuberculous disease in whom it was of extent large enough to provide material for research and who had not undergone any form of active treatment other than actual operation, such as scraping. That the required number was obtained was largely due to the help of Dr. J. H. Sequeira, the majority of the cases having first come under his observation.

EXPERIMENTAL ANIMALS.

Very little need be said in regard to the various experimental animals beyond what has been stated in the Second Interim Report. The same methods continued to be used for obtaining bovine animals ; these in all cases came from Jersey and were personally selected and purchased there by Mr. Keddie. The reasons for using Jersey cattle almost exclusively for experimental purposes have already been explained, the chief of them being the circumstance that according to available information tuberculous disease among cattle in the island was either non-existent or extremely rare.

The fowls and pigeons used in the investigation of avian tuberculosis and for other experiments were obtained in almost every instance locally, there being no reason to suspect the prevalence at any time of epidemic or other disease amongst the poultry in the district. From every group of birds purchased some were set aside and kept as controls.

The quarantine station at Isleworth for dogs and monkeys was continued till it was no longer required for providing healthy animals of those species. At no time were experiments of any kind performed at Isleworth, the only work other than the careful observation of the stock animals kept there being the post-mortem and microscopic examination of such of them as died or were killed on account of obvious or suspected disease, or for the purpose of control observations.

THREE SUBORDINATE INVESTIGATIONS AT STANSTED.

Three separate investigations were undertaken at Stansted during the course of other work which, although done with the approval of the Commission and in one instance by their direction, are not referred to in the Final Report. In all three the experiments were of a preliminary nature and not sufficiently extended to enable definite conclusions to be drawn from them. The details of all of them are set out in the Appendix.

(1) *Immunity.*

The slight amount of disease produced in bovine animals by the tubercle bacillus of the human type and the possibility of utilising this resistance to one form of tuberculosis for the artificial production of an immunity to the disease readily set up in these animals by the bovine tubercle bacillus, frequently engaged the attention of the Commission during the first three or four years of their inquiry. But the great amount of investigatory work that had to be done in connection with the questions more strictly comprised within the terms of Reference precluded devotion of much time and labour to matters only indirectly concerned with tuberculosis in man.

Nevertheless, early in 1906 it was decided to carry out some tentative experiments with a limited number of calves to ascertain whether these animals could be immunised against bovine tuberculosis by previous inoculation either with large doses of feebly virulent human tubercle bacilli or with small doses of tubercle bacilli such as had already proved highly virulent to bovines. A definite scheme of procedure in this sense was drawn up after careful consideration, and the actual experiments were carried out during the following nine months by the Investigators at Stansted. The preliminary inoculations with the human viruses were performed by Dr. Cobbett at Blythwood Farm, the calves so inoculated being transferred to Walpole later on, while still apparently in perfect health. The vaccinations with bovine viruses as well as all subsequent resistance-test inoculations on both classes of calves were performed at Walpole by Drs. A. Stanley Griffith and F. Griffith, and these two Investigators submitted a report to the Commission on the results obtained. This report, together with full details of the investigation, is included in the third volume of the Appendix.

It is sufficient to say here that the experiments showed that by the inoculation of large doses of human tubercle bacilli, as also by vaccination with small doses of living bovine tubercle bacilli, the calf can in many instances be enabled to resist the inoculation at a later period of a dose of bovine tubercle bacilli which otherwise would have set up in it severe and fatal tuberculosis. None of the above vaccinated animals was allowed to live for a longer period after the resistance-test inoculation than three months, and though in all of them some disease was found on post-mortem examination, in the great majority it was of a slight and non-progressive character.

In certain of the animals, however, resistance in this sense was not produced, calves that had been vaccinated once and even twice with slightly virulent tubercle bacilli developed some of them severe tuberculosis when inoculated with virulent bovine bacilli. The necessarily limited scope of these preliminary experiments did not provide sufficient data on which to found any opinion as to the probable duration of any resistance that might have been produced in the protected animals.

The results of these experiments were fully considered by the Commissioners after their Second Interim Report had been presented, and they decided that though the facts obtained were of considerable importance, the number of animals included in the investigation was not sufficient to enable any general conclusions to be safely drawn from them. They were unanimously of the opinion that further experiments on immunity should be carried out on a much larger scale if this were possible. Such experiments, they considered, should extend over a period of time considerably longer than that occupied by the preliminary inquiry, and should include at least 100 bovine animals. But it was eventually decided that such an extended investigation, though likely to be of great scientific and practical value, could not conveniently be undertaken by a temporary body such as a Royal Commission. The difficulty of obtaining a sufficient number of healthy calves of like age, the provision of the necessary accommodation without interfering with other investigations at Walpole, and above all the time that would have to be occupied and the heavy expense that would be involved compelled the Commission to give up the idea of carrying the investigation on immunity beyond the stage arrived at, and whilst desiring that the account of the experiments should be included in their Appendix, they themselves express no opinion as to the significance of the results so recorded.

(2) *Human Milk.*

From time to time during the course of other work at Blythwood careful observations were made on pregnant heifers by Dr. Cobbett to note the effect of inoculation of tubercle bacilli in bringing about tuberculous infection of the mammary gland and in influencing the production naturally of tuberculosis in the calves of which they were subsequently delivered; he also demonstrated the infectiveness of their milk when this secretion became established.

The results of these observations were recorded by him in the third volume of the Appendix to the Second Interim Report, the main facts being tabulated on pages 250–253. The tables showed that of five heifers infected with tuberculosis by means of subcutaneous inoculation, their milk, when the secretion had become established, was infective to guinea-pigs in two instances; that in two of the five the mammary glands were found to be tuberculously affected when the animals were killed; and that of the five calves produced by these heifers three yielded post-mortem evidence of tuberculosis of the hepatic glands, contracted presumably before birth.

An investigation was carried out by Dr. F. Griffith on the excretion of tubercle bacilli in the milk of naturally infected tuberculous cows showing no disease of the udder. This inquiry and the details of the experiments formed the subjects of the Third Interim Report and Appendix. About the same time Dr. A. Stanley Griffith carried out a series of experiments to determine whether after experimentally introducing tubercle bacilli into the blood-stream of healthy cows or heifers these bacilli could pass from the blood into the milk without producing changes in the mammary tissue. Of the eleven experiments performed nine showed that the normal mammary tissue will permit of the escape of tubercle bacilli into the milk after the bacilli have obtained access to the blood-stream in sufficient quantities. The details of this investigation are fully given in Volume III. of the Appendix to this Report, page 81.

As a result of the consideration of these facts it became a matter of some interest to inquire whether the milk of a lactating woman, suffering from tuberculosis, might be a possible source of danger to her infant, a question to which conflicting answers have been given by different authorities, but regarding which very few reliable observations appear to have been experimentally made. Such an investigation was not practicable on a large scale, the matter not being one strictly included in the Reference, and pressure of other work together with the difficulty of obtaining suitable cases prevented more than a very few being examined. But the milk of four nursing women was tested by Dr. A. Stanley Griffith. Briefly it may be stated that each of these women was suffering from pulmonary tuberculosis, though not in an acute form. The diagnosis in each case had been made before the patient was selected, but in only one of the four cases did the woman's sputum produce tuberculosis when injected into guinea-pigs. The results of the inoculation of guinea-pigs with milk from these women were negative in all the four cases. The details of this investigation are recorded in Vol. I. of the Appendix to this Report (pages 12, 18 and 104–5). The investigation was of course too limited to enable any deductions to be drawn from it.

(3) *Action of Light-Rays on Lupus Bacilli.*

Dr. A. Stanley Griffith carried out some preliminary observations with the object of obtaining information as to how the undoubted benefit caused by treating lupus by light-rays is produced. The experiments were made with lupus tubercle bacilli isolated at Blythwood and grown on artificial media prepared there. The exposures of these cultures to the light-rays were made in the skin department of the London Hospital by permission of Dr. Sequeira and with his co-operation. The results are recorded in Vol. II. of the Appendix to this Report (page 9). They show that the growth of the tubercle bacillus is inhibited by both Finsen and Kromeyer rays, but the limited scope of the investigation did not supply any evidence as to whether this effect is produced by a bactericidal action of the rays on the bacilli or by some modification brought about by the rays in the artificial media or living tissue in which they were growing.

INVESTIGATIONS OTHER THAN THOSE AT STANSTED.

Two separate investigations, not carried out in the laboratories of the Commission, remain to be noted ; both of them were referred to in the Second Interim Report as having been undertaken but at that time unfinished. The results in each case were not sufficiently definite to enable the Commission to make use of them, and neither is referred to in the present final Report.

The first was an experimental investigation undertaken by Dr. James Miller, of Birmingham, at the request of the Commission.

Various means were being sought at that time to determine any differences that might exist between tubercle bacilli of the human and bovine types apart from their pathogenic effects on cattle and rabbits, and the work entrusted to Dr. Miller was to observe the changes that occurred on bringing living tubercle bacilli obtained from different sources into contact with living cells, and to note if any constant differences could be seen between the interactions of leucocytes with bacilli of these two types.

The cultures of tubercle bacilli with which the investigation was to be carried out were supplied from the Stansted laboratories, but the whole of the experimental work connected with it was done at Birmingham. Four strains in all were used, three being of bovine and one of human origin ; but unfortunately this last virus was subsequently found to be bovine not human in type, and, therefore, no deductions could be drawn from Dr. Miller's observations as to any contrasts in the cellular reaction induced by different types of tubercle bacillus. But he noted that although practically no difference was observed with regard to either the nature of the cells taking part in the primary reaction or in the amount of this reaction between any of the four viruses, certain minor variations, such as the duration of a period of quiescence, the formation of the giant-cell follicle and the degree of the secondary inflammatory reaction could be clearly noted in several cases. Thus though the cellular reaction was not uniform with every virus, either in point of time or effect, these variations appeared to be merely an expression of the slight and unimportant differences not infrequently to be observed in virulence among different strains of bovine tubercle bacilli towards the calf and rabbit.

Apart from the question of differences between tubercle bacilli of the two types, Dr. Miller made careful observations of the general cellular reaction following injection of cultures of living tubercle bacilli into guinea-pigs which are of great interest in connection with Dr. Eastwood's histological examinations of dead tissues. They may be briefly summarised as follows :—

1. A period of inflammatory reaction, during which the bacilli are ingested by cells.
2. A period of quiescence, when the bacilli disappear almost entirely.
3. A period when the bacilli reappear and are enclosed within giant-cell follicles, a condition accompanied by a second inflammatory reaction. These giant-cell follicles may persist or may break down, in which latter case there is a marked increase in the inflammatory reaction.

Dr. Miller's investigation was carried out with great skill and minute care. Further observations were not undertaken on similar lines, Dr. Eastwood's histological researches having shown that there is an essential identity between the lesions caused by the bovine tubercle bacillus and those produced by the human type.

The second of these two separate investigations, referred to at page 48 of the Second Interim Report, was in the nature of a statistical inquiry, undertaken in 1904-5, with a view to obtain data more trustworthy than are supplied by "Causes of Death, Officially Certified," as to the extent of abdominal tuberculosis amongst the population generally. The method of inquiry adopted, which took as its basis a systematic examination of post-mortem records at hospitals, has already been described in the Report in question, and reason given for deeming the results which were being obtained as likely to prove of little value for the purposes of the Commission. Subsequent examination of the records collected has confirmed this view. Want of detail in the majority of hospital post-mortem records examined precluded exclusion of the possibility of lesions having been present in organs not specifically stated to have been healthy, while the lack of uniformity in the methods of making and recording post-mortem examinations in different places, as well as the different plans of procedure carried out from time to time in one and the same hospital, prevented any general conclusions as to the proportion of abdominal tuberculosis to other forms of that disease.

During the time that the experimental work was being carried out at Stansted a very large number of tuberculin tests of healthy and infected bovine and other animals was made by the resident investigators and the results systematically recorded. The number of tests actually made and the wide range of different species of animals tested make these records of considerable value, and it is proposed to publish an abstract of the facts obtained and the opinions of the investigators thereon in a supplemental volume of the Appendix to this Report. The procedure adopted for testing the non-infected animals was explained in the Second Interim Report (page 43).

At the end of this Report will be found a list of the contents of all the Reports and Appendices presented by the Commission. In this connection it is important to note that the method of this Commission has differed profoundly from the procedure usually adopted by Royal Commissions. The work has consisted entirely of a scientific research carried out under the direction and supervision of the Commission by experts at farms and laboratories devoted solely to the purpose. No witnesses have been examined, and therefore the only evidence on which the Commission's reports are based is the accumulated facts resulting from the experimental work done. During the progress of any investigation it was obviously improper that the facts coming to light should from time to time be made public in the precise order in which they were being revealed. But throughout these researches minute record has been kept of each step of experimental work, so that after Report by the Commission the fullest detail of all proceedings embodied in Appendix volumes might be available for independent judgment on fact irrespective of interpretation of fact that may have been indulged in by the Commissioners. To the same end a completely representative collection of pathological specimens carefully prepared and preserved in the course of the Commission's researches has been delivered to the

Royal College of Surgeons for permanent exhibition in the Museum of that institution.

As in Appendices to the Second Interim Report so in Appendices to this their Final Report, the Commissioners have regarded it as right and proper to encourage their Investigators each to set out not only the multitudinous facts arising from his work, but also his own views as to the bearing of the results of that work on the problems before the Commission.

No account of the practical administration of the work of the Commission, however brief, would be complete without reference to the help received from the Stationery Office, the Office of Works, and the officials of the Treasury, especially Mr. H. T. Holmes who throughout assisted the Secretary with the purely financial business.

LIST OF REPORTS AND APPENDICES PRESENTED BY THE ROYAL COMMISSION ON TUBERCULOSIS (HUMAN AND BOVINE).

First Interim Report.

Presented in May 1904.

No Appendix.

Second Interim Report.

Presented January 1907.

Appendix.—In four volumes.

VOLUME I.—The Pathogenic Effects of Bovine Viruses:

The Numerical Estimation of Tubercle Bacilli.
The Table of Origins of thirty Bovine Viruses.
Inoculation Experiments on Bovines, Goats, Pigs, Chimpanzees, Monkeys, and Lemurs.
Descriptive Charts of the Experiments with each Virus, and full Post-Mortem Notes of the larger experimental animals.
Inoculation Experiments on Dogs, Cats, the Mongoose and Hedgehog, Rabbits, Guinea-pigs, Rats, and Mice.
Detailed description and summaries of Feeding Experiments.
Plates: Photographs of Lesions produced in Bovine and other animals.

VOLUME II.—The Pathogenic Effects of Human Viruses:

The Table of Origins of sixty-two Human Viruses.
Descriptive Charts of the Experiments with each Virus, and full Post-Mortem Notes of the larger experimental animals; together with a history of the patient from which each Virus was obtained.
A Consideration of the Virulence of different strains of Tubercle Bacilli obtained from man for various species of animals; viz., Bovines, Rabbits, Guinea-pigs, Goats, Pigs, Monkeys, Baboons, Chimpanzees, Dogs, Cats, Rats, Mice, and Fowls; together with Tables of the Experiments made on each Species.
The Relative Susceptibility of Different Species of Animals to Tubercle Bacilli of Human and Bovine Origin.
Plates: Photographs of Lesions produced in Bovine and other animals.

VOLUME III.—Additional Investigations of Bovine and Human Viruses.

1. The Cultural Characters of the Bovine Tubercle Bacillus (with Plates).
2. The Cultural Characters of the Tubercle Bacilli obtained from Man.
3. Supplementary Report on the Cultivation of Tubercle Bacilli obtained from Man.
4. Report on the Changes in Reaction produced in Broth by Human and Bovine Tubercle Bacilli.
   - (*a*) The Changes in Reaction produced in Glycerin-broth.
   - (*b*) Additional Observations on the Changes in Reaction produced in Glycerin-broth.
   - (*c*) The Changes in Reaction produced in Glucose-broth.
   - (*d*) The Changes in Reaction produced in Glycerinated Litmus Milk.

VOLUME III.—*continued.*

5. Modification Experiments with Tubercle Bacilli of Bovine Origin.
   - (*a*) Modification by Culture.
   - (*b*) Modification by Animal Passage.
   - (*c*) Influence of Glycerin on Virulence.
6. Report on the Stability of Virulence of the Tubercle Bacillus of Human Origin in Artificial Culture, including the Influence of Glycerin in Culture Media.
   - (*a*) The Virulence of Tubercle Bacilli from Cultures and in Emulsions of Tuberculous Animal Tissues compared.
   - (*b*) Does long-continued Cultivation on Artificial Media attenuate the Tubercle Bacillus?
   - (*c*) The Influence of Glycerin in Culture Media.
7. Report on the minute non-progressive tubercles found in Calves injected with Tubercle Bacilli of Human Origin which are unable to provoke a progressive infection in this Species of Animal.
8. Report on the Distribution of Non-virulent Tubercle Bacilli of Human Origin in the body of the Calf after Subcutaneous Injection.
9. Report on the Dissemination of Tubercle Bacilli in Different Species of Animals after Subcutaneous Inoculation.
10. Report on the Influence of Individual Susceptibility and of Dose on the Severity of an Experimental Infection by Tubercle Bacilli of Human Origin.
    - (*a*) The Variation in the Capacity for resisting Tuberculosis among Individuals of the same Species.
    - (*b*) The Influence of Lactation.
    - (*c*) The Influence of Dose.
11. Report on Congenital Tuberculosis at Blythwood Farm.

VOLUME IV.—Comparative Histological and Bacteriological Investigations on the Relationship of Human and Bovine Tuberculosis:

Part I.—General Report on the Histological and Bacteriological Investigations.
Part II.—Comparative Histology.
Part III.—Comparative Bacteriology.

Third Interim Report.

Presented January 1909.

Appendix.—(Included in the Report volume).

The Results of Inoculation and Feeding Experiments made with the Faeces and Milk of naturally Tuberculous Cattle.

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Full Post-Mortem Notes of the naturally infected Cows, and details of the investigations.

Final Report.

Presented 1911.

Appendix.—In seven volumes.

VOLUME I.—Investigation of Viruses obtained from Cases of Human Tuberculosis (other than Lupus):

General Results of the Investigation of 55 Cases of Human Tuberculosis.
Charts showing extent and distribution of disease in Cases of Tuberculosis in Children primary in the Alimentary Tract.
The Investigation of the Cultural Characteristics of 54 Viruses.

VOLUME I.—*continued.*

Consideration of the effects produced in Different Species of Animals by the Inoculation of Human Tubercle Bacilli and Bovine Tubercle Bacilli of Human Origin; and of the effects produced by feeding.
Modification Experiments with Human Tubercle Bacilli. (Detailed description of the Experiments and consideration of the Results obtained.)
Table of Origins of the Viruses investigated.
Detailed History of each Case, and Summaries of Experimental Results.
Details of the Experiments.
Plates: Photographs of some of the Cultures.

VOLUME II.—Investigation of Viruses obtained from Cases of Lupus:

Consideration of the cultural characters and pathogenicity of the Cultures isolated.
Classification of the Lupus Viruses according to cultural characters and virulence.
Tabular Summary of the Results of the Passage Experiments.
Table of Origins of the Lupus Viruses.
Detailed History of each Case and Summaries of Experimental Results.
Details of the Experiments.
Plates: Photographs of some of the Lupus Cultures.

VOLUME III.—Reports on Investigations dealing with:—

1. Certain Human Viruses of Irregular Type:

(*a*) Results of the Further Investigation of Cultures from the Viruses placed in Group III. (*see* 2nd Interim Report, page 30).
(*b*) Results of the Special Investigation of two of the Group III. Cultures (H 13. "A.D." (Calf 301), and H 49. "T.C.") which exhibited exceptional features.
(*c*) Results of the Special Investigation of the two Cultures H 60. "W.B." (Bronchial Gland) and H 90. "I.P." (Retroperitoneal Gland), isolated since the 2nd Interim Report, which exhibited the features of the two Group III. Cultures.
Plates: Photographs of Cultures.

2. The Excretion of Tubercle Bacilli:

(*a*) In the Milk of Cows and Goats.
(*b*) Into the Undeveloped Udder.

3. Investigation of Tubercle Bacilli from Cases of Swine Tuberculosis:

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4. Report on Immunity Experiments.

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(i.) The Stability of Virulence of Tubercle Bacilli in the Living Animal, and
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1. Investigation of Tubercle Bacilli derived from Tuberculosis occurring naturally in the Horse:

General Results of Experiments with cultures from the original material, and of passage experiments; and consideration of cultural characters.
Table of Origins of the Equine Viruses.
Summaries of Results of Inoculation Experiments with each Virus; and Details of the Experiments.
Plate: Photographs of Cultures of Bovine and Equine Tubercle Bacilli.

2. Investigation of Viruses obtained from five cases of Casual Tuberculosis of various Mammals:

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3. Investigation of Avian Tubercle Bacilli obtained from Birds and Swine:

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Cultural Characters of the Avian Tubercle Bacillus.
Summaries of the Results of the Experiments on different species of animals; and Details of the Experiments.
Plate: Photograph of Cultures of Avian, Human and Bovine Tubercle Bacilli.

Volume IV.—*continued.*

4. Modification Experiments with Tubercle Bacilli derived from Animals other than Man :

   Summary of Results.
   - (*a*) Experiments with Avian Tubercle Bacilli.
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